RE: 09/942,435, Structure Search
Please do an structure search on the elected echinocandin species of page 3 (attached); wherein:

R1, R2, R3, R6, R7, R8, and R10 = OH;

R4, R5, and R11 = CH3;

R9 = H; and

R= STRUCTURE P. 3

I. IF ELECTED STRUCTURE IS FOUND (I ASSUME IT'S OUT THERE, OR ANOTHER SPECIES, SINCE CLAIMS ARE DRAWN TO METHOD), PLEASE SEARCH FOLLOWING TERMS WITH IT:

granules, pharmaceutical, carbohydrate, echinocandin (claim 1 terms)

AND
1 fructose; (claim 5-6)
2 water, saline, acetone; and (claim 7)
3 mannitol (claim 9-11)

*IF SOME/ALL OF THE ABOVE TERMS, FROM GROUPS I-III ARE NOT FOUND, PLEASE SEARCH THE OTHER SPECIES LISTED IN CLAIMS 5 & 6 (which can be either the carbohydrate or the granular diluent).

II. IF THE ELECTED STRUCTURE IS NOT FOUND; PLEASE SEARCH THE SPECIES OF CLAIMS 2-4, PAGE 5-7, UNTIL A STRUCTURE IS EITHER FOUND OR NOT FOUND. **IF NOT FOUND, END SEARCH.**

III. IF ANOTHER SPECIES IS FOUND, OTHER THAN THAT ELECTED, PLEASE SEARCH WITH SAME TERMS AS ABOVE:

granules, pharmaceutical, carbohydrate, echinocandin (claim 1 terms)

AND
1 fructose; (claim 5-6)
2 water, saline, acetone; and (claim 7)
3 mannitol (claim 9-11)

*IF SOME/ALL OF THE ABOVE TERMS, FROM GROUPS I-III ARE NOT FOUND, PLEASE SEARCH THE OTHER SPECIES LISTED IN CLAIMS 5 & 6 (which can be either the carbohydrate or the granular diluent).

158936-46-0P 158936-47-1P 158936-48-2P 158936-49-3P
158936-50-6P 158936-51-7P 158936-52-8P 158936-53-9P
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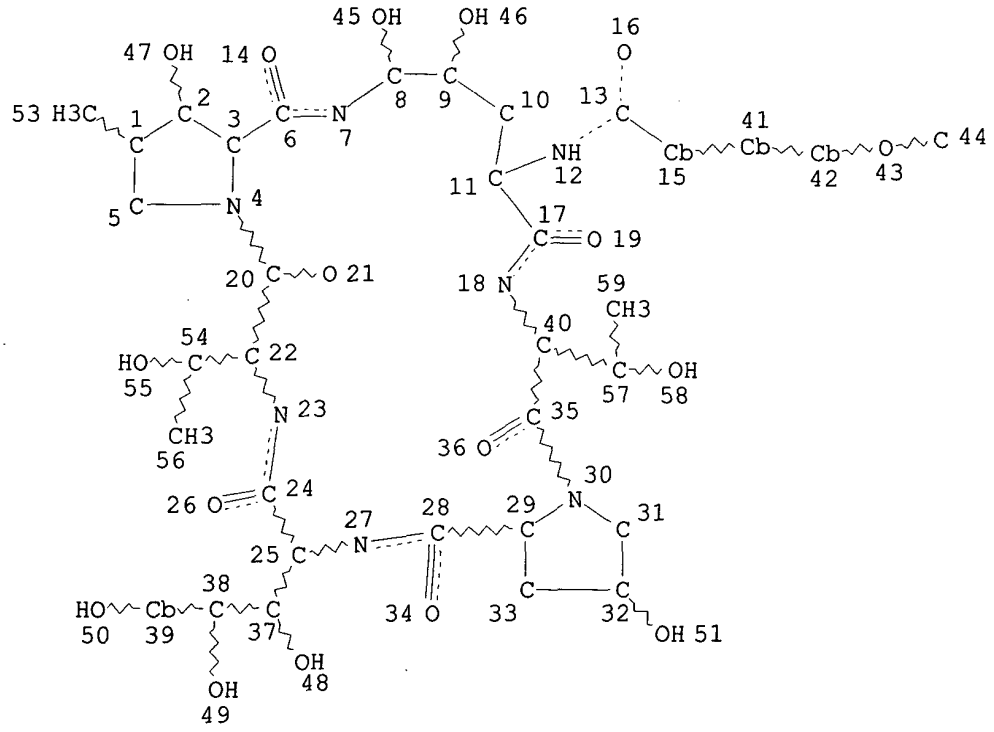
158936-62-0P 158936-63-1P 158936-64-2P 158936-65-3P
158936-66-4P 158936-67-5P 158936-68-6P 158936-69-7P
158936-70-0P 158936-71-1P 158936-72-2P 158936-73-3P
158936-74-4P 158936-75-5P 158936-76-6P 158936-77-7P
158936-78-8P 158936-79-9P 158936-80-2P 158936-81-3P
158936-82-4P 158936-83-5P 158936-84-6P 158936-85-7P
158936-86-8P 158936-87-9P 158936-88-0P 158936-89-1P
158936-90-4P 158936-91-5P 159000-67-6P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of, as medical fungicide)

IT 107-08-4, 1-Iodopropane 107-82-4 110-53-2, 1-Bromopentane 111-66-0, 1-Octene 536-74-3 540-38-5, 4-Iodophenol 542-69-8, 1-Iodobutane 619-44-3, Methyl 4-iodobenzoate 629-05-0, 1-Octyne 638-45-9, 1-Iodohexane 693-02-7, 1-Hexyne 764-93-2, 1-Decyne 1066-54-2 1647-26-3, 1-Bromo-2-cyclohexylethane 2038-91-7 2346-07-8 2527-99-3, Methyl 5-bromofuran-2-carboxylate 3034-86-4 6661-54-7 13295-53-9, Cyclobutylmethyl tosylate 21856-53-1, Cyclopentylmethyl tosylate 29558-77-8 60834-63-1 62124-28-1 63619-51-2 63619-63-6 63619-64-7 108366-80-9 141430-54-8 158407-15-9 158937-74-7 158937-75-8 158937-76-9 158937-77-0 158937-78-1 158937-79-2 158937-80-5 158937-81-6 158937-82-7 158937-83-8 158937-84-9 158937-85-0
RL: RCT (Reactant); RACT (Reactant or reagent)
(reaction of, in prepn. of cyclic peptide deriv medical fungicide)

IT 79404-91-4, Cilofungin
RL: RCT (Reactant); RACT (Reactant or reagent)
(reaction of, in prepn. of medical fungicide)

(FILE 'CASREACT' ENTERED AT 15:07:03 ON 06 JUN 2003)
L35 STR



NODE ATTRIBUTES:
DEFAULT MLEVEL IS ATOM
MLEVEL IS CLASS AT 15 39 41 42
GGCAT IS UNS AT 15
GGCAT IS UNS AT 39
GGCAT IS UNS AT 41
GGCAT IS UNS AT 42
DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:
RING(S) ARE ISOLATED OR EMBEDDED
NUMBER OF NODES IS 58

STEREO ATTRIBUTES: NONE
L38 3 SEA FILE=CASREACT SSS FUL L35 (6 REACTIONS)

100.0% DONE 156 VERIFIED 6 HIT RXNS 3 DOCS
SEARCH TIME: 00.00.01

L38 ANSWER 1 OF 3 CASREACT COPYRIGHT 2003 ACS
ACCESSION NUMBER: 132:308664 CASREACT
TITLE: Photochemical process for conversion of the 1,2-diol moiety of an echinocandin compound to the 1-deoxy-2-keto analog
INVENTOR(S): Hitchcock, Stephen Andrew; Gregory, George Stuart
PATENT ASSIGNEE(S): Eli Lilly and Company, USA
SOURCE: PCT Int. Appl., 28 pp.

CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000024694	A1	20000504	WO 1999-US25301	19991027

W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.: US 1998-105936P 19981028
OTHER SOURCE(S): MARPAT 132:308664

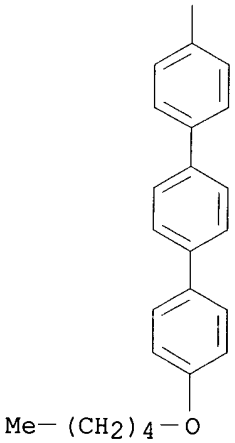
AB A method for converting an epoxy or hydroxy moiety to a 1-deoxy-2-keto moiety is described which includes: (1) reacting a compd. having an epoxy or hydroxy moiety with a thiophenol and (2) irradiating the 1-phenylthio-2-hydroxy moiety with UV or near-UV radiation to convert the 1-phenylsulfide-2-hydroxy moiety to a 1-deoxy-2-keto moiety. The process was used to modify the cyclic peptide ring system of an echinocandin-type compd. contg. a 1,2-diol moiety to produce new keto analogs.

102(e) < 1 yr. B/F Look for terms ~~operation~~ w/

RX(1) OF 3 **A** + B ===> C...

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

PAGE 2-A



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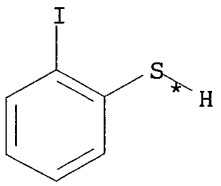
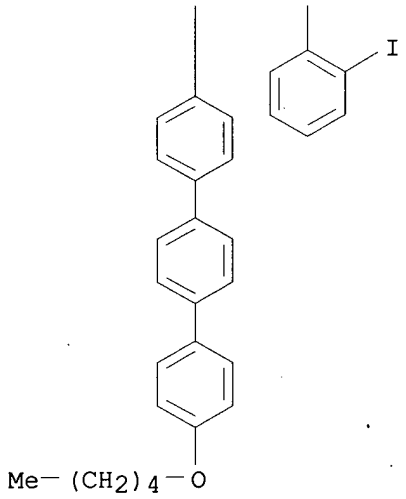


B (1) →

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

PAGE 2-A



C

RX(1) RCT A **166663-25-8**, B 37972-89-7
PRO C 266317-25-3
SOL 75-05-8 MeCN, 67-56-1 MeOH
REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L38 ANSWER 2 OF 3 CASREACT COPYRIGHT 2003 ACS
ACCESSION NUMBER: 129:276286 CASREACT
TITLE: Studies on the phosphorylation of LY303366
AUTHOR(S): Udodong, Uko E.; Turner, William W.; Astelford, Bret A.; Brown, Frank, Jr.; Clayton, Marcella T.; Dunlap, Steven E.; Frank, Scott A.; Grutsch, John L.; LaGrandeur, Lisa M.; Verral, Daniel E.; Werner, John A.
CORPORATE SOURCE: Lilly Research Laboratories, Lilly Corporate Center, Indianapolis, IN, 46285, USA
SOURCE: Tetrahedron Letters (1998), 39(34), 6115-6118

Searcher : Shears 308-4994

First for making compound & Indicate Cards W/

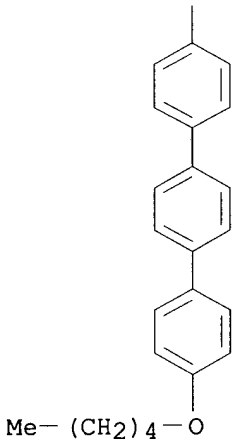
CODEN: TELEAY; ISSN: 0040-4039
PUBLISHER: Elsevier Science Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English
GI

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

AB Phosphorylation of LY303366 was studied in THF and DMF. Benzyl phosphate (I) could be prepd. in excellent yield using LiOH as the base. Both I and the derived phosphonic acid monosodium salt were prone to undergo hydrolytic dephosphorylation.

RX(1) OF 1 **A** + B ===> C

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *



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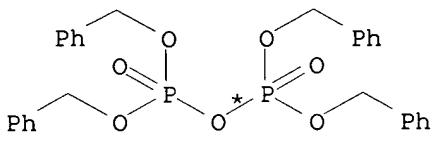

B

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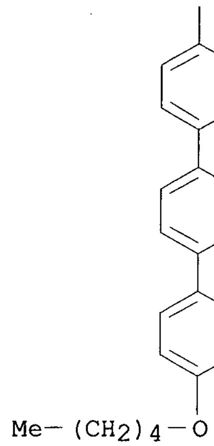
* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

PAGE 2-A



C
YIELD 33%

```
RX(1)      RCT  A 166663-25-8, B 990-91-0
           RGT  D 1310-65-2 LiOH
           PRO  C 213669-65-9
           SOL  75-09-2 CH2Cl2, 109-99-9 THF
REFERENCE COUNT:         6     THERE ARE 6 CITED REFERENCES AVAILABLE FOR
                               THIS RECORD. ALL CITATIONS AVAILABLE IN
                               THE RE FORMAT
```

L38 ANSWER 3 OF 3 CASREACT COPYRIGHT 2003 ACS

ACCESSION NUMBER:	126:212437 CASREACT
TITLE:	Preparation of cyclic peptide antifungal agents
INVENTOR(S):	Rodriguez, Michael John
PATENT ASSIGNEE(S):	Lilly, Eli, and Co., USA
SOURCE:	Eur. Pat. Appl., 22 pp. CODEN: EPXXDW
DOCUMENT TYPE:	Patent
LANGUAGE:	English
FAMILY ACC. NUM. COUNT:	1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 757058	A1	19970205	EP 1996-305345	19960722
EP 757058	B1	20001108		
R: AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LI, LU, NL, PT, SE				
US 5629289	A	19970513	US 1995-506790	19950725
AT 197460	E	20001111	AT 1996-305345	19960722
ES 2151638	T3	20010101	ES 1996-305345	19960722
WO 9705163	A1	19970213	WO 1996-US12111	19960723
W: AL, AM, AU, AZ, BB, BG, BR, BY, CA, CN, CZ, EE, GE, HU, IL, IS, JP, KE, KG, KP, KR, KZ, LK, LR, LS, LT, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, RO, RU, SD, SG, SI, SK, TJ, TM, TR,				

TT, UA, UG, US, UZ
RW: KE, LS, MW, SD, SZ, UG, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG

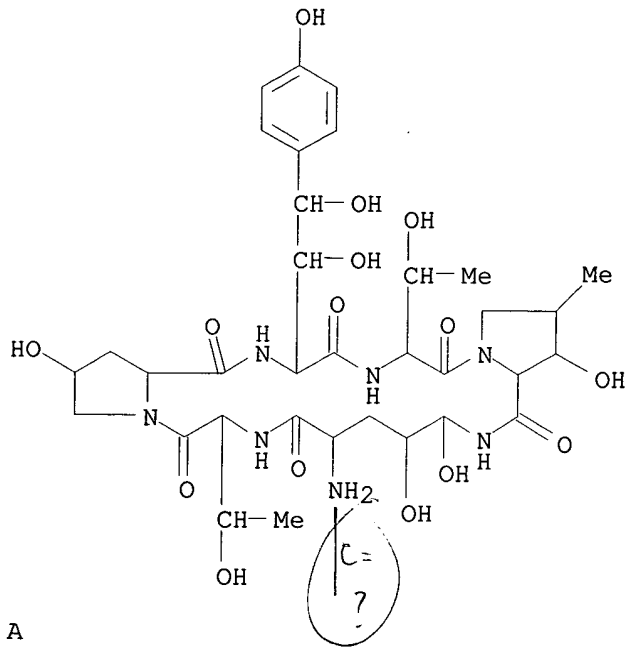
AU 9665938	A1	19970226	AU 1996-65938	19960723
JP 11510165	T2	19990907	JP 1996-507687	19960723
PRIORITY APPLN. INFO.:			US 1995-506790	19950725
			WO 1996-US12111	19960723

OTHER SOURCE(S): MARPAT 126:212437
GI

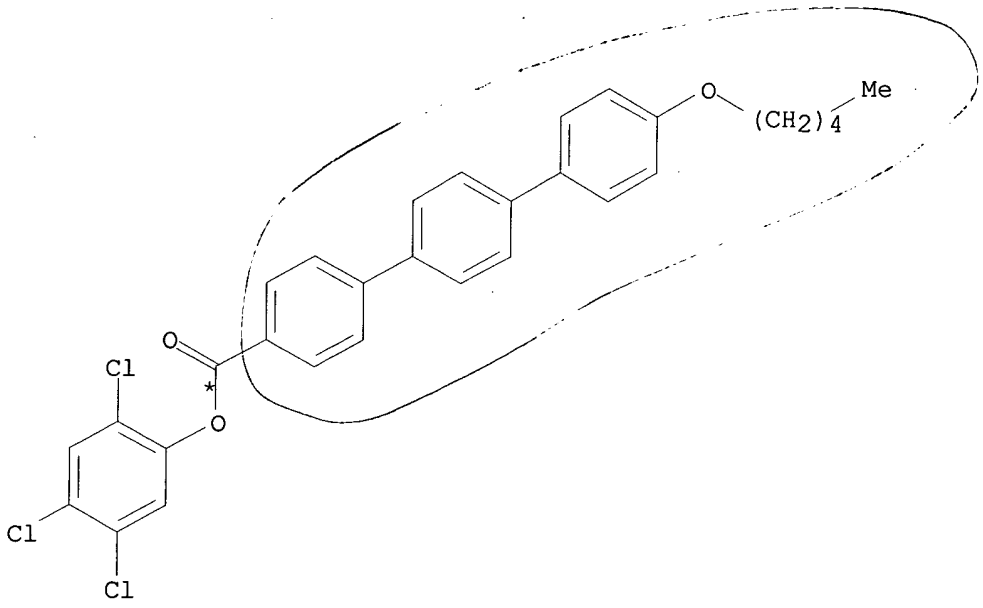
* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

AB Provided are pharmaceutical formulations, and methods of inhibiting fungal and parasitic activity using cyclopeptides I [R11 = H, CH2OH, CHMeOH, CH(OH)CH2CONH2; R12 = H, CH2OH, CHMeOH; R13 = H, Me; R31 = H, OH, OR30; R30 = C1-6 alkyl, PhCH2, (CH2)2SiMe3, CH2CH:CH2, CH2CH(OH)CH2OH, (CH2)aCO2H, (CH2)bNR41R42, (CH2)cPOR43R44, (CH2CH2O)d(C1-6)alkyl; a, b, c = 1-6; R41, R42 = H, C1-6 alkyl; R41R42 = (CH2)e; R43, R44 = OH, C1-6 alkoxy; d = 1, 2; e = 3-5; R32, R21, R22, R23, R24 = OH, H; R0 = OH, OPO3H2, OP(O)(OH)R1, OP(O)(OH)OR1, R1 = C1-6 alkyl, Ph, p-halophenyl, p-nitrophenyl, PhCH2, p-halobenzyl, p-nitrobenzyl; R2 = COC6H4R3; R3 = C6H4R5-4, C.tplbond.CC6H4R6-4, p-C6H4C.tplbond.CC6H4R7-4, p-C6H4C6H4R8-4; R5, R6, R7, R8 = H, C1-12 alkyl, C2-12 alkynyl, C1-12 alkoxy, C1-12 alkylthio, halo, O(CH2)m[O(CH2)n]pO(C1-12 alkyl), O(CH2)qXR4; m = 2-4; n = 2-4; p = 0, 1; q = 2-4; X = pyrrolidino, piperidino, piperazino; R4 = H, C1-12 alkyl, C3-12 cycloalkyl, benzyl, C3-12 cycloalkylmethyl; with the proviso that at least 1 of R11 and R12 must be H] or pharmaceutically acceptable salt thereof. Thus, acylation of 348.1 g (60.2 mmol) antibiotic A 30912A nucleus with 26.0 g (48.2 mmol) terphenyl active ester Me(CH2)4O-p-C6H4-p-C6H4-p-C6H4CO2C6H2Cl3-2,4,5 in 8.5 L of DMF gave 18 g acylated deriv. II (R11 = R12 = CHMeOH, R31 = R32 = OH) (III). Treatment of 5 g III with 17 mL CF3CO2H and 35 mL Et3SiH in 250 mL CH2Cl2 gave 3.872 g (79%) reduced deriv. II (R11 = R12 = CHMeOH, R31 = R32 = H), which underwent retro-aldol condensation by treatment with 2.51 g (22.6 mmol) Me3N+O- in 20 mL of a 1:1 mixt. of MeCN and DMF at 100.degree. for 24 h to give 72% II (R11 = R12 = R31 = R32 = H). Pharmaceutical formulations contg. II (R11 = R12 = R31 = R32 = H) arte given.

RX(1) OF 6 A + B ===> C...



A



B

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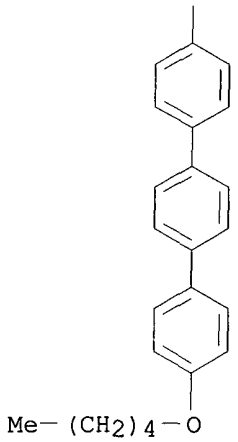
* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

Searcher : Shears 308-4994

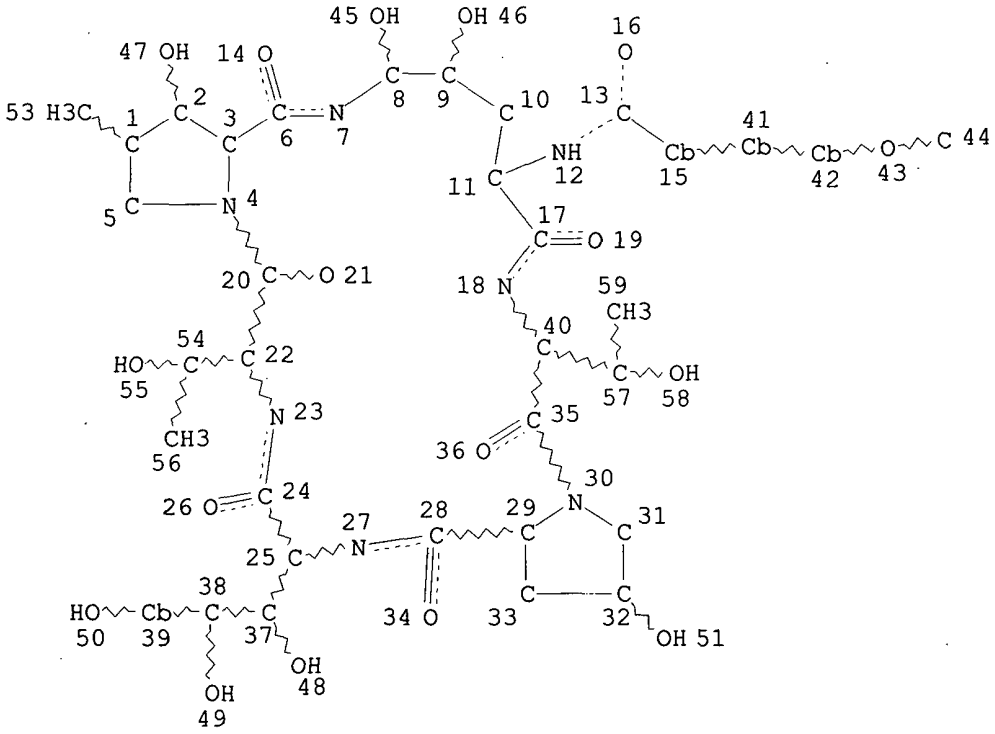


C

RX(1) RCT A 79411-15-7, B 158937-65-6
PRO C **166663-25-8**
SOL 68-12-2 DMF

(FILE 'DJSMDS, CHEMINFORMRX' ENTERED AT 15:08:16 ON 06 JUN 2003)

L35 STR



NODE ATTRIBUTES:
DEFAULT MLEVEL IS ATOM
MLEVEL IS CLASS AT 15 39 41 42
GGCAT IS UNS AT 15
GGCAT IS UNS AT 39
GGCAT IS UNS AT 41
GGCAT IS UNS AT 42
DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:
RING(S) ARE ISOLATED OR EMBEDDED
NUMBER OF NODES IS 58

STEREO ATTRIBUTES: NONE
L39 0 SEA L35

FILE 'HOME' ENTERED AT 15:17:42 ON 06 JUN 2003

(1,3)-beta-D-glucan synthase. The antifungal efficacy and safety of LY303366 were investigated in treatment and prophylaxis of primary pulmonary aspergillosis due to Aspergillus firmigatus in persistently neutropenic rabbits. Treatment study groups sere either not treated (controls) or treated with amphotericin B (AmB) at 1 mg/kg of body weight per day or with LY303366 at 1, 5, 10, and 20 mg/kg/day. In rabbits treated with LY303366, there was a significant improvement in survival and a reduction in organism-mediated pulmonary injury measured by the number of infarcts, total lung weight, and ultrafast computerized tomography scan pulmonary lesion score. Rabbits receiving prophylactic LY303366 also demonstrated significant improvement in survival and reduction in organism-mediated pulmonary injury. AmB and LY303366 had comparable therapeutic efficacies by all parameters with the exception of reduction in tissue burden of A. fumigatus, where AmB was superior to LY303366. LY303366 demonstrated a dose-dependent effect on hyphal injury with progressive truncation, swelling, and vacuolization. LY303366 administered in single doses of 1, 5, 10, and 20 mg/kg demonstrated dose-proportional increases in the maximum concentration of drug in plasma and the area under the concentration-time curve from 0 to 72 h with no changes in plasma drug clearance. The 1-mg/kg dosage maintained plasma drug levels above the MIC for 18 h, and dosages of greater than or equal to 5 mg/kg maintained plasma drug levels above the MIC for the entire 24-h dosing interval. There was no significant elevation of the concentrations of hepatic transaminases or creatinine in serum in LY303366-treated rabbits. In summary, LY303366 improved survival and decreased pulmonary injury with no apparent toxicity in the treatment and prevention of invasive pulmonary aspergillosis in persistently neutropenic rabbits.

L12 ANSWER 27 OF 38 EMBASE COPYRIGHT 2003 ELSEVIER SCI. B.V.
ACCESSION NUMBER: 1998097055 EMBASE
TITLE: Progress in fighting systemic fungal infections in haematological neoplasia.
AUTHOR: De Pauw B.E.; Meis J.F.G.M.
CORPORATE SOURCE: Dr. B.E. De Pauw, Department of Haematology, University Hospital St. Radboud, P.O. Box 9101, NL-6500 HB Nijmegen, Netherlands
SOURCE: Supportive Care in Cancer, (1998) 6/1 (31-38).
Refs: 55
ISSN: 0941-4355 CODEN: SCCAEO
COUNTRY: Germany
DOCUMENT TYPE: Journal; General Review
FILE SEGMENT: 004 Microbiology
016 Cancer
037 Drug Literature Index
038 Adverse Reactions Titles
LANGUAGE: English
SUMMARY LANGUAGE: English
AB Considering the limited data available, there is clearly a need for thorough, well-designed clinical research on the epidemiology, diagnosis, treatment and prevention of invasive fungal infection in patients who are treated for cancer. Our knowledge has increased, but the information obtained so far is patchy and not generally applicable, as it is influenced by local problems and circumstances. New diagnostic tools have become available, but they are still insufficient in many cases. Until the value of the presently

available chemoprophylaxis has been established beyond doubt, the strategy should be one of wait-and-see for patients with a low or moderate risk of developing infection. In bone marrow transplant recipients fluconazole has shown favourable results in eliminating yeast infections, but in patients at high risk of mould infections early initiation of intravenous treatment with amphotericin B at a therapeutic dose remains the best approach. The question of the optimal time point to start empirical antifungal treatment remains and has even been extended by the dispute about what antifungal drugs should be used for this purpose. Amphotericin B is still the drug of choice for the treatment of disseminated fungal infection, but its lipid formulations seem to offer a safer, though far more expensive, alternative. Head-to-head comparisons between the different formulations are required before a final conclusion on their respective efficacies and toxicities can be drawn, and it is questionable whether a higher dose will produce better results. Fluconazole appears very useful against the majority of Candida infections, whereas itraconazole is effective against both yeast and moulds, providing that adequate resorption can be ensured. The results of the first clinical trial of voriconazole in pulmonary aspergillosis have proved very promising.

L12 ANSWER 28 OF 38 EMBASE COPYRIGHT 2003 ELSEVIER SCI. B.V.
ACCESSION NUMBER: 97137175 EMBASE
DOCUMENT NUMBER: 1997137175
TITLE: In vitro activity of a new **echinocandin**, LY303366, compared with those of amphotericin B and fluconazole against clinical yeast isolates.
AUTHOR: Uzun O.; Kocagoz S.; Cetinkaya Y.; Arikan S.; Unal S.
CORPORATE SOURCE: O. Uzun, Section of Infectious Diseases, Department of Medicine, Hacettepe Univ. School of Medicine, Ankara 06100, Turkey. ou01-k@servis2.net.tr
SOURCE: Antimicrobial Agents and Chemotherapy, (1997) 41/5 (1156-1157).
Refs: 11
ISSN: 0066-4804 CODEN: AMACCQ
COUNTRY: United States
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 004 Microbiology
037 Drug Literature Index
LANGUAGE: English
SUMMARY LANGUAGE: English
AB The in vitro activity of LY303366, a new **echinocandin** derivative, was evaluated with 191 yeast isolates by a broth microdilution method. The MICs at which 50% of the isolates were inhibited were 0.125 .mu.g/ml for Candida albicans and C. tropicalis, 0.25 .mu.g/ml for C. krusei, C. kefyr, and C. glabrata, and 2.0 .mu.g/ml for C. parapsilosis.

L12 ANSWER 29 OF 38 EMBASE COPYRIGHT 2003 ELSEVIER SCI. B.V.
ACCESSION NUMBER: 97101461 EMBASE
DOCUMENT NUMBER: 1997101461
TITLE: Antifungal agents in the 1990s. Current status and future developments.
AUTHOR: Kauffman C.A.; Carver P.L.
CORPORATE SOURCE: Dr. C.A. Kauffman, Veterans Affairs Medical Center, 2215 Fuller Road, Ann Arbor, MI 48105, United States. ckauff@umich.edu

SOURCE: Drugs, (1997) 53/4 (539-549).
Refs: 109
ISSN: 0012-6667 CODEN: DRUGAY
COUNTRY: New Zealand
DOCUMENT TYPE: Journal; General Review
FILE SEGMENT: 004 Microbiology
030 Pharmacology
037 Drug Literature Index
039 Pharmacy
038 Adverse Reactions Titles
LANGUAGE: English
SUMMARY LANGUAGE: English

AB Significant advances in antifungal therapy have occurred in the last decade. Most of these advances have been tied to the introduction of the triazoles, itraconazole and fluconazole. Itraconazole has proved efficacious for the treatment of subacute to chronic infections with the endemic mycoses and other opportunistic filamentous fungi, including Aspergillus spp. Fluconazole is now routinely used for mucocutaneous and systemic candidiasis, and its use for coccidioidal meningitis has obviated the need for intrathecal amphotericin B in most patients. Large, well controlled trials in AIDS patients with cryptococcal meningitis have shown the benefit of induction therapy with amphotericin B and flucytosine, followed by consolidation and life-long maintenance therapy with fluconazole. Concomitant with the increased use of these well tolerated, effective oral triazole agents has come the emergence of drug resistance in AIDS patients and shifts in the species of yeasts causing infection in hospitalised patients. Amphotericin B remains the drug of choice for many fungal infections, especially those that are life-threatening. Lipid-containing formulations of amphotericin B have recently been approved: these preparations significantly reduce the risk of amphotericin B-induced nephrotoxicity. Several new fungicidal agents are currently in early trials. With the increasing number of available antifungal drugs, future studies will help define the appropriate niche for each and the possible benefit of therapy with combinations of drugs.

L12 ANSWER 30 OF 38 EMBASE COPYRIGHT 2003 ELSEVIER SCI. B.V.

ACCESSION NUMBER: 97244841 EMBASE
DOCUMENT NUMBER: 1997244841
TITLE: Candidiasis: Implications for intensivists and pulmonologists.
AUTHOR: Gelfand M.S.
CORPORATE SOURCE: Dr. M.S. Gelfand, 188 S. Bellevue, Memphis, TN 38104, United States
SOURCE: Seminars in Respiratory and Critical Care Medicine, (1997) 18/3 (225-234).
Refs: 86
ISSN: 1069-3424 CODEN: SRCCEX
COUNTRY: United States
DOCUMENT TYPE: Journal; Conference Article
FILE SEGMENT: 004 Microbiology
006 Internal Medicine
037 Drug Literature Index
038 Adverse Reactions Titles
LANGUAGE: English
SUMMARY LANGUAGE: English

AB The incidence of invasive candidiasis has increased markedly in

recent years in immunocompromised and intensive care patients. High morbidity, mortality, and economic cost of candidiasis; limited sensitivity of available diagnostic techniques, outbreaks of Candida cross-infection in surgical and ICU patients, emergence of non-albicans Candida species, and increase in antifungal resistance are some of the major developments reviewed in this paper. New diagnostic techniques and therapeutic agents and strategies are being developed for the management of serious Candida infections.

L12 ANSWER 31 OF 38 EMBASE COPYRIGHT 2003 ELSEVIER SCI. B.V.
ACCESSION NUMBER: 97184682 EMBASE
DOCUMENT NUMBER: 1997184682
TITLE: Treatment of Pneumocystis carinii pneumonia in adults with AIDS.
AUTHOR: Deresinski S.C.
CORPORATE SOURCE: Dr. S.C. Deresinski, Division of Infectious Diseases, Santa Clara Valley Medical Center, 751 S. Bacom Ave., San Jose, CA 95128, United States
SOURCE: Seminars in Respiratory Infections, (1997) 12/2 (79-97).
Refs: 142
ISSN: 0882-0546 CODEN: SRINES
COUNTRY: United States
DOCUMENT TYPE: Journal; General Review
FILE SEGMENT: 004 Microbiology
015 Chest Diseases, Thoracic Surgery and Tuberculosis
026 Immunology, Serology and Transplantation
037 Drug Literature Index
038 Adverse Reactions Titles
LANGUAGE: English
SUMMARY LANGUAGE: English
AB Trimethoprim-sulfamethoxazole remains the treatment of choice in patients with Pneumocystis carinii pneumonia (PCP) requiring intravenous therapy. Those patients who require intravenous therapy who cannot tolerate or who fail therapy with trimethoprim-sulfamethoxazole may be treated with either pentamidine or trimetrexate (plus folinic acid), with or without orally administered dapsone. The toxicity of the former drug makes trimetrexate-based therapy the preferred second choice for parenteral use. Treatment with trimethoprim-sulfamethoxazole, dapsone-trimethoprim, or clindamycin-primaquine is approximately of equivalent efficacy, but variable toxicity, inpatients with mild to moderate PCP for whom an oral route of administration is appropriate. Atovaquone, formulated as an oral suspension, is also effective, but, in the absence of additional data, must be considered as second line therapy. Adjunctive corticosteroid therapy is indicated for patients with [PAO2 - Pao2] more than 30 mm Hg or Pao2 less than 60 mm Hg while breathing ambient air in the absence of contraindications. Recognition of the apparent fungal nature of P carinii as well as improved understanding of the pathophysiology of PCP will lead to further improvements in antipneumocystis therapy.

L12 ANSWER 32 OF 38 WPIDS (C) 2003 THOMSON DERWENT
ACCESSION NUMBER: 1996-105901 [11] WPIDS
DOC. NO. CPI: C1996-033560
TITLE: Extracellular expression of proteins in S.lividans - using regulatory signals from the Xanthobacter

agilis phthalyl amidase gene.
DERWENT CLASS: B04 D16
INVENTOR(S): QUEENER, S W; ZOCK, J M
PATENT ASSIGNEE(S): (ELIL) LILLY & CO ELI
COUNTRY COUNT: 65
PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
WO 9602637	A1	19960201	(199611)*	EN	49
RW: AT BE CH DE DK ES FR GB GR IE IT KE LU MC MW NL OA PT SD SE SZ UG					
W: AM AT AU BB BG BR BY CA CH CN CZ DE DK EE ES FI GB GE HU IS JP KE KG KP KR KZ LK LR LT LU LV MD MG MN MW MX NO NZ PL PT RO RU SD SE SG SI SK TJ TM TT UA UG UZ VN					
AU 9530981	A	19960216	(199622)		
ZA 9505900	A	19970326	(199718)		48
US 5658755	A	19970819	(199739)		24

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
WO 9602637	A1	WO 1995-US8832	19950714
AU 9530981	A	AU 1995-30981	19950714
ZA 9505900	A	ZA 1995-5900	19950714
US 5658755	A	US 1994-275487	19940715

FILING DETAILS:

PATENT NO	KIND		PATENT NO
AU 9530981	A	Based on	WO 9602637

PRIORITY APPLN. INFO: US 1994-275487 19940715
AN 1996-105901 [11] WPIDS
AB WO 9602637 A UPAB: 19960315
A novel method for expressing a protein comprising: (a) positioning a nucleotide sequence encoding the protein in a DNA vector adjacent to and downstream from a signal peptide functional in Streptomyces lividans (SL); (b) transforming a host cell with the vector; and (c) culturing the host cell for gene expression, whereby the protein is secreted in soluble form.

USE - The method can be used to produce proteins such as haemoglobin, alpha-, beta- or gamma-interferon, erythropoietin, **granulocyte**-colony stimulating factor, interleukin (IL)-1, IL-3, tissue plasminogen activator, epidermal growth factor, Factor XIII, Met-Phe-trypsinogen, procarboxypeptidase B, Lys(B28)Pro(B29)-proinsulin, Met-Arg-proinsulin or **echinocandin** B deacylase (claimed).

ADVANTAGE - The method enables the host to produce and secrete soluble, properly-folded, functional proteins in an amt. in excess of the amt. of a cell-bound form produced by the natural source of the protein.

Dwg.0/3
ABEQ US 5658755 A UPAB: 19970926
A method for expressing protein, said method comprising:

a) positioning a nucleotide sequence encoding said protein in a

DNA vector adjacent to and downstream from a nucleotide sequence encoding a 42 amino acid signal peptide (sequence given in the specification) functional in Streptomyces lividans;

b) transforming a host cell with said vector; and

c) culturing said host cell under conditions suitable for gene expression, whereby said protein is secreted in soluble form.

Dwg.0/3

L12 ANSWER 33 OF 38 EMBASE COPYRIGHT 2003 ELSEVIER SCI. B.V.
ACCESSION NUMBER: 96048954 EMBASE
DOCUMENT NUMBER: 1996048954
TITLE: Antifungal agents: Chemotherapeutic targets and immunologic strategies.
AUTHOR: Georgopapadakou N.H.; Walsh T.J.
CORPORATE SOURCE: Department of Molecular Biology, Princeton University,Princeton, NJ 08544-1014, United States
SOURCE: Antimicrobial Agents and Chemotherapy, (1996) 40/2 (279-291).
ISSN: 0066-4804 CODEN: AMACCQ
COUNTRY: United States
DOCUMENT TYPE: Journal; (Short Survey)
FILE SEGMENT: 004 Microbiology
026 Immunology, Serology and Transplantation
030 Pharmacology
037 Drug Literature Index
LANGUAGE: English

L12 ANSWER 34 OF 38 EMBASE COPYRIGHT 2003 ELSEVIER SCI. B.V.
ACCESSION NUMBER: 96358506 EMBASE
DOCUMENT NUMBER: 1996358506
TITLE: Fungal infections in patients undergoing bone marrow transplantation: An approach to a rational management protocol.
AUTHOR: Casstagnola E.; Bucci B.; Montinaro E.; Viscoli C.
CORPORATE SOURCE: Divisione Malattie Infettive, Istituto G Gaslini, Large G Gaslini 5,16148 Genova, Italy
SOURCE: Bone Marrow Transplantation, (1996) 18/SUPPL. 2 (97-106).
ISSN: 0268-3369 CODEN: BMTRE
COUNTRY: United Kingdom
DOCUMENT TYPE: Journal; Conference Article
FILE SEGMENT: 004 Microbiology
016 Cancer
025 Hematology
030 Pharmacology
037 Drug Literature Index
038 Adverse Reactions Titles
LANGUAGE: English
SUMMARY LANGUAGE: English

AB Candida sp. and Aspergillus sp. are the most common fungal pathogens causing infection in bone marrow transplant recipients and represent an increasing cause of morbidity and mortality. At this time there is no generally accepted rule for the antifungal management of these complications. Antifungal drugs in immunocompromised patients are usually administered for prophylaxis, for therapy of specific infections or for empirical or preemptive therapy. The present article reports schedules of administrations and pediatric and adult dosages of the main antifungal drugs presently available,

(fluconazole, itraconazole, amphotericin B deoxycholate, lipid formulations of amphotericin B and flucytosine), together with their spectrum of action and main toxicities. Thereafter, the available information about prevention and treatment of fungal infections in bone marrow transplant recipients is summarized. Briefly, fluconazole remains the drug of choice for prevention of Candida infections in bone marrow transplant recipients, while itraconazole has been seldomly used for this indication, due to erratic oral absorption. However, new itraconazole formulations are being studied, that might disclose new clinical perspectives, due to improved bioavailability. The duration of prophylaxis is still an open issue. Resistance to the new azoles may become a problem in the near future. For this reason, it is likely that the approach to the use of these new drugs should be similar to the one commonly used for antibacterial drugs, i.e. based on pathogen-related, drug-related and host-related factors. Mainly due to lack of diagnostic tools, very little studies have been performed for prevention of aspergillosis. Available data seem to show that there might be a role for low-dose intravenous amphotericin B, which has shown to be effective for secondary prophylaxis. Itraconazole and intranasal amphotericin B have been studied, as well. Although fluconazole and itraconazole (in the rare instances in which the oral route is reliable) can also have therapeutic indications, both for empirical and for specific therapy, amphotericin B (with or without flucytosine) remains the main therapeutic option. New antifungal drugs and new supportive strategies role of hematopoietic growth factors) are in the research pipeline and will hopefully disclose new perspectives in the near future.

L12 ANSWER 35 OF 38 EMBASE COPYRIGHT 2003 ELSEVIER SCI. B.V.
ACCESSION NUMBER: 94317362 EMBASE
DOCUMENT NUMBER: 1994317362
TITLE: [Therapeutic prospects in invasive aspergillosis]. PERSPECTIVES MEDICAMENTEUSES DANS LE TRAITEMENT DE L'ASPERGILLOSE INVASIVE.
AUTHOR: Yeni P.
CORPORATE SOURCE: Service de Medecine Interne, Hopital Bichat, 46, Rue Henri Huchard,75018 Paris, France
SOURCE: Pathologie Biologie, (1994) 42/7 (700-705).
ISSN: 0369-8114 CODEN: PTBIAN
COUNTRY: France
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 004 Microbiology
030 Pharmacology
037 Drug Literature Index
LANGUAGE: French
SUMMARY LANGUAGE: French; English
AB The frequency of infections caused by Aspergillus sp. is on the rise, and the mortality is high in the disseminated forms of the disease. Amphotericin B is theoretically the gold standard treatment, but remains inefficient in severely immunocompromised patients, particularly bone-marrow transplants. The interest of lipidic formulations of amphotericin B, triazoles, new antifungal drugs targeted on the fungal cell wall and immunomodulators is discussed.

L12 ANSWER 36 OF 38 EMBASE COPYRIGHT 2003 ELSEVIER SCI. B.V.
ACCESSION NUMBER: 93322856 EMBASE

DOCUMENT NUMBER: 1993322856
TITLE: Prevention of invasive fungal infections in patients with neoplastic diseases.
AUTHOR: Walsh T.J.; Lee J.W.
CORPORATE SOURCE: Infectious Diseases Section, National Cancer Institute, Building 10,Bethesda, MD 20892, United States
SOURCE: Clinical Infectious Diseases, (1993) 17/SUPPL. 2 (S468-S480).
ISSN: 1058-4838 CODEN: CIDIEL
COUNTRY: United States
DOCUMENT TYPE: Journal; Conference Article
FILE SEGMENT: 004 Microbiology
016 Cancer
037 Drug Literature Index
038 Adverse Reactions Titles
LANGUAGE: English
SUMMARY LANGUAGE: English

AB Invasive fungal infections are important causes of morbidity and mortality among patients with neoplastic diseases, particularly those with protracted **granulocytopenia**, those receiving corticosteroids, and those undergoing allogeneic bone marrow transplantation. These mycoses are often difficult to diagnose early, and their treatment is frequently unsuccessful. Antifungal compounds have been used in studies of a variety of preventive strategies including prophylaxis, early empirical therapy, empirical therapy, and secondary prophylaxis. Among all compounds studied thus far, fluconazole has demonstrated the most promising activity in prevention of invasive candidiasis, particularly in adult allogeneic bone marrow transplant recipients. However, fluconazole does not have activity at currently approved dosages against Candida krusei, Torulopsis glabrata, and most filamentous fungi, including Aspergillus species. Empirically administered amphotericin B significantly decreases the frequency of invasive fungal infections in persistently or recurrently febrile **granulocytopenic** patients. The use of itraconazole for prevention of aspergillosis warrants study. The current lack of reliable preventive regimens against infections due to Aspergillus and against those due to several emerging fungal pathogens presents an ongoing challenge. The use of recombinant human cytokines, transfusion of effector cells, and administration of newer antifungal compounds are new potential modalities for prevention of invasive mycoses.

L12 ANSWER 37 OF 38 MEDLINE DUPLICATE 3
ACCESSION NUMBER: 92223273 MEDLINE
DOCUMENT NUMBER: 92223273 PubMed ID: 1562687
TITLE: Experimental antifungal chemotherapy in **granulocytopenic** animal models of disseminated candidiasis: approaches to understanding investigational antifungal compounds for patients with neoplastic diseases.
AUTHOR: Walsh T J; Lee J W; Roilides E; Francis P; Bacher J; Lyman C A; Pizzo P A
CORPORATE SOURCE: Infectious Diseases Section, Pediatric Branch, National Cancer Institute, Bethesda, Maryland 20892.
SOURCE: CLINICAL INFECTIOUS DISEASES, (1992 Mar) 14 Suppl 1 S139-47. Ref: 59
Journal code: 9203213. ISSN: 1058-4838.

PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
(REVIEW, TUTORIAL)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199205
ENTRY DATE: Entered STN: 19920607
Last Updated on STN: 19920607
Entered Medline: 19920519

AB Disseminated candidiasis is the most common life-threatening invasive fungal infection in **granulocytopenic** patients. A review of recent approaches to pre-clinical laboratory investigation of promising antifungal compounds, which may have potential utility in **granulocytopenic** patients is presented. A particularly useful strategy is the study of persistently **granulocytopenic** rabbit models of acute, subacute, and chronic forms of disseminated candidiasis. When the antifungal triazoles (fluconazole, itraconazole, and SCH 39304 [SCH 42427]) were each evaluated for use as preventive, early treatment, or delayed treatment in the different models, the triazoles were consistently more active when used for preventive and early treatment than for delayed treatment. These triazoles were as active as amphotericin B plus flucytosine (AB + FC) when used for early treatment but were less active than AB + FC when used for delayed treatment. Several lipid formulations of amphotericin B demonstrate reduced nephrotoxicity at higher safely achievable dosages in comparison to those of deoxycholate amphotericin B in several models of disseminated candidiasis. When administered to follow non-linear saturable Michaelis-Menten-type plasma pharmacokinetics, the antifungal activity of the **echinocandin** compound cilofungin was significantly augmented. Thoughtfully designed and carefully conducted laboratory investigations in appropriate animal models of disseminated candidiasis can provide a scientific foundation and guide for development of clinical protocols investigating new approaches to prevention and treatment of invasive candidiasis in **granulocytopenic** patients.

L12 ANSWER 38 OF 38 MEDLINE
ACCESSION NUMBER: 86300189 MEDLINE
DOCUMENT NUMBER: 86300189 PubMed ID: 3527633
TITLE: Cell wall of pathogenic yeasts and implications for antimycotic therapy.
AUTHOR: Cassone A
SOURCE: DRUGS UNDER EXPERIMENTAL AND CLINICAL RESEARCH, (1986) 12 (6-7) 635-43.
Journal code: 7802135. ISSN: 0378-6501.
PUB. COUNTRY: Switzerland
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 198610
ENTRY DATE: Entered STN: 19900321
Last Updated on STN: 19900321
Entered Medline: 19861023

AB Yeast cell wall is a complex, multilayered structure where amorphous, **granular** and fibrillar components interact with

each other to confer both the specific cell shape and osmotic protection against lysis. Thus it is widely recognized that as is the case with bacteria, yeast cell wall is a major potential target for selective chemotherapeutic drugs. Despite intensive research, very few such drugs have been discovered and none has found substantial application in human diseases to date. Among the different cell wall components, beta-glucan and chitin are the fibrillar materials playing a fundamental role in the overall rigidity and resistance of the wall. Inhibition of the metabolism of these polymers, therefore, should promptly lead to lysis. This indeed occurs and aculeacin, **echinocandin** and polyoxins are examples of agents producing such an action. Particular attention should be focused on chitin synthesis. Although quantitatively a minor cell wall component, chitin is important in the mechanism of dimorphic transition, especially in Candida albicans, a major human opportunistic pathogen. This transition is associated with increased invasiveness and general virulence of the fungus. Yeast cell wall may also limit the effect of antifungals which owe their action to disturbance of the cytoplasmic membrane or of cell metabolism. Indeed, the cell wall may hinder access to the cell interior both under growing conditions and, particularly, during cell ageing in the stationary phase, when important structural changes occur in the cell wall due to unbalanced wall growth (phenotypic drug resistance).

FILE 'HCAPLUS' ENTERED AT 14:55:25 ON 06 JUN 2003
L13 0 S L5 AND LEVULOSE

FILE 'MEDLINE, BIOSIS, EMBASE, WPIDS, CONFSCI, SCISEARCH, JICST-EPLUS, JAPIO' ENTERED AT 14:55:51 ON 06 JUN 2003
L14 0 S L13

(FILE 'HCAPLUS, MEDLINE, BIOSIS, EMBASE, WPIDS, CONFSCI, SCISEARCH, JICST-EPLUS, JAPIO' ENTERED AT 14:56:18 ON 06 JUN 2003)
L15 26 S "SCHWIER J"?/AU
L16 28678 S "TAYLOR J"?/AU
L17 2 S L15 AND L16
L18 2 S (L15 OR L16) AND L5
L19 2 S L17 OR L18
L20 1 DUP REM L19 (1 DUPLICATE REMOVED)

L20 ANSWER 1 OF 1 HCAPLUS COPYRIGHT 2003 ACS DUPLICATE 1
ACCESSION NUMBER: 2000:627958 HCAPLUS
DOCUMENT NUMBER: 133:227789
TITLE: Processes for making pharmaceutical oral **echinocandin** formulations and compositions
INVENTOR(S): **Schwier, John Richard; Taylor, Jerry**
PATENT ASSIGNEE(S): Eli Lilly and Company, USA
SOURCE: PCT Int. Appl., 40 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

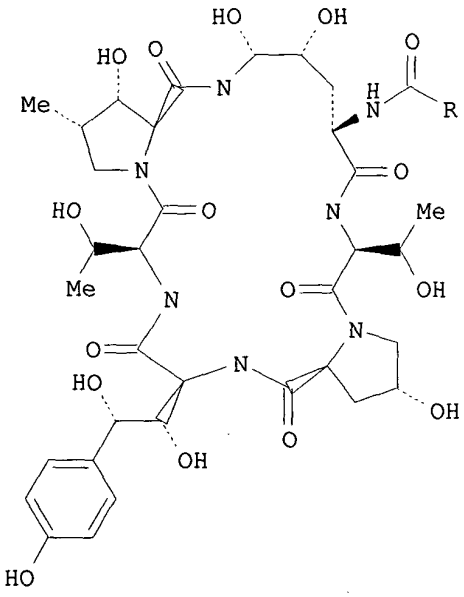
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE

WO 2000051567	A1	20000908	WO 2000-US5547	20000302	
W:	AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, GM, HR, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW:	GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
EP 1156784	A1	20011128	EP 2000-912160	20000302	
R:	AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
BR 2000008713	A	20011226	BR 2000-8713	20000302	
JP 2002538097	T2	20021112	JP 2000-602036	20000302	
US 2002151474	A1	20021017	US 2001-942435	20010829	

PRIORITY APPLN. INFO.: US 1999-122693P P 19990303
WO 2000-US5547 W 20000302

OTHER SOURCE(S): MARPAT 133:227789

GI



I

AB A fluid bed spray process is described where one or more carbohydrates are incorporated into an **echinocandin** formulation to provide a significant improvement in thermal stability. The carbohydrate is solubilized with an **echinocandin** compd. or **echinocandin**/carbohydrate complex in a solvent(s) to form a pharmaceutical soln. which is sprayed onto the surface of a granular diluent or carrier. Alternatively, a granulating agent is added to the pharmaceutical soln. which is then sprayed onto the surface of a non-granular diluent or carrier. I was prepd., and a fructose complex with I

also prepd.
REFERENCE COUNT: 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

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                E ECHINOCANCIN/CN 5
                E ECHINOCANDIN/CN 5
L40           2 S E3-E4

     FILE 'HCAPLUS' ENTERED AT 15:09:40 ON 06 JUN 2003
L1            1 SEA FILE=REGISTRY ABB=ON  PLU=ON  ECHINOCANDIN/CN
L3            1 SEA FILE=REGISTRY ABB=ON  PLU=ON  183211-59-8/RN
L4            2 SEA FILE=REGISTRY ABB=ON  PLU=ON  L1 OR L3
L40           2 SEA FILE=REGISTRY ABB=ON  PLU=ON  (ECHINOCANDIN/CN OR
                "ECHINOCANDIN B"/CN)
L41         382 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L4 OR L40 OR ECHINOCANDI
                N OR ECB(S)ECHINOCANDIN
L42           5 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L41 AND (POWDER? OR
                GRANUL?)



L1            1 SEA FILE=REGISTRY ABB=ON  PLU=ON  ECHINOCANDIN/CN
L2            2 SEA FILE=REGISTRY ABB=ON  PLU=ON  FRUCTOSE/CN
L3            1 SEA FILE=REGISTRY ABB=ON  PLU=ON  183211-59-8/RN
L4            2 SEA FILE=REGISTRY ABB=ON  PLU=ON  L1 OR L3
L40           2 SEA FILE=REGISTRY ABB=ON  PLU=ON  (ECHINOCANDIN/CN OR
                "ECHINOCANDIN B"/CN)
L41         382 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L4 OR L40 OR ECHINOCANDI
                N OR ECB(S)ECHINOCANDIN
L43           3 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L41 AND (L2 OR FRUCTOSE
                OR LEVULOSE)


L44           0 S (L42 OR L43) NOT L8

     (FILE 'MEDLINE, BIOSIS, EMBASE, WPIDS, CONFSCI, SCISEARCH,
     JICST-EPLUS, JAPIO' ENTERED AT 15:15:17 ON 06 JUN 2003)
L45          45 S L42
L46           3 S L43
L47           0 S (L45 OR L46) NOT L11

     (FILE 'HCAPLUS, MEDLINE, BIOSIS, EMBASE, WPIDS, CONFSCI, SCISEARCH,
     JICST-EPLUS, JAPIO' ENTERED AT 15:16:42 ON 06 JUN 2003)
L48           2 S (L15 OR L16) AND L41
L49           0 S L48 NOT L19

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L21 (FILE 'REGISTRY' ENTERED AT 14:57:48 ON 06 JUN 2003)
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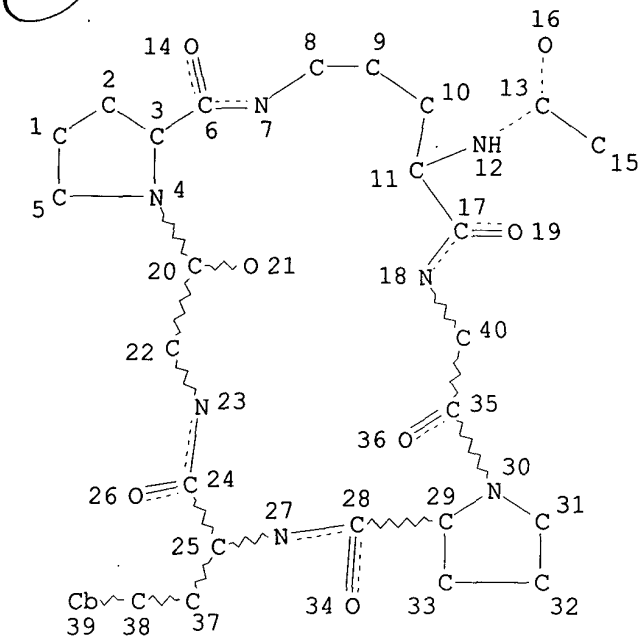

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NSPEC IS RC AT 15
DEFAULT MLEVEL IS ATOM
GGCAT IS UNS AT 39
DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:
RING(S) ARE ISOLATED OR EMBEDDED
NUMBER OF NODES IS 40

STEREO ATTRIBUTES: NONE
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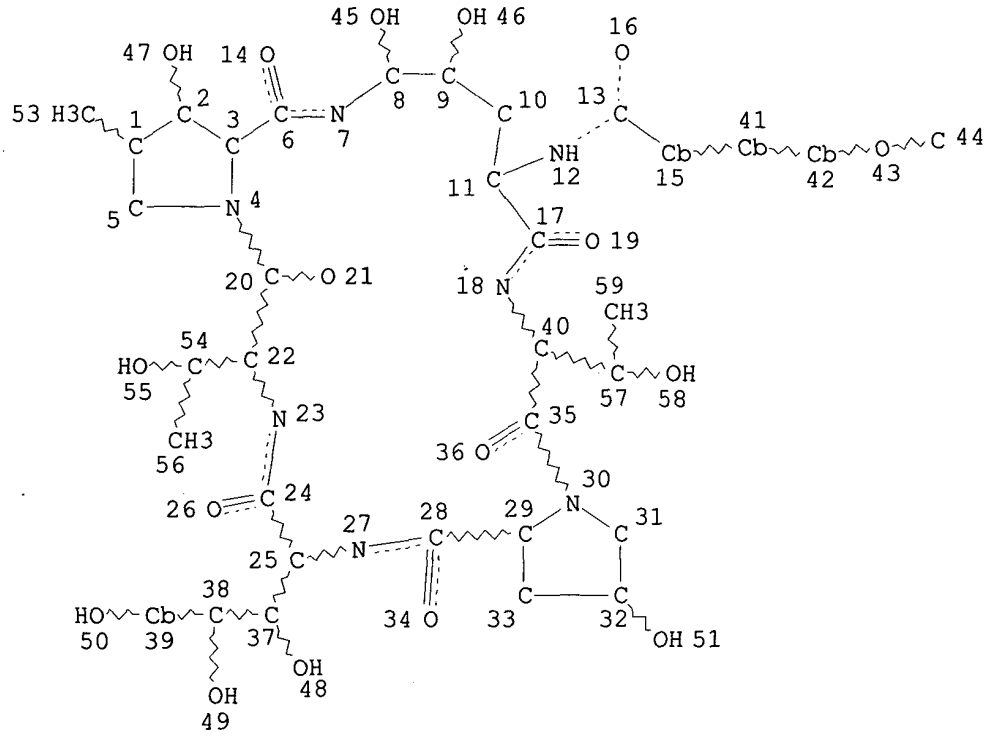
L27 STR



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DEFAULT MLEVEL IS ATOM
GGCAT IS UNS AT 15
GGCAT IS UNS AT 39
GGCAT IS UNS AT 41
GGCAT IS UNS AT 42
DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:
RING(S) ARE ISOLATED OR EMBEDDED
NUMBER OF NODES IS 58

STEREO ATTRIBUTES: NONE
L28 64 SEA FILE=REGISTRY SUB=L22 SSS FUL L27

100.0% PROCESSED 1627 ITERATIONS 64 ANSWERS
SEARCH TIME: 00.00.01

FILE 'HCAPLUS' ENTERED AT 15:00:42 ON 06 JUN 2003
L29 70 S L28
L30 23 S L29 NOT (PY=>1999 OR PD=>19990303)
L31 23 S L30 NOT L8

? No L8

E1 THROUGH E7 ASSIGNED

L31 ANSWER 1 OF 23 HCAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 1998:719842 HCAPLUS
DOCUMENT NUMBER: 130:75801

TITLE: Antifungal efficacy, safety, and single-dose pharmacokinetics of LY303366, a novel echinocandin B, in experimental pulmonary aspergillosis in persistently neutropenic rabbits

AUTHOR(S): Petraitis, Vidmantas; Petraitiene, Ruta; Groll, Andreas H.; Bell, Aaron; Callender, Diana P.; Sein, Tin; Schaufele, Robert L.; McMillian, Carl L.; Bacher, John; Walsh, Thomas J.

CORPORATE SOURCE: Immunocomprornised Host Section, Pediatric Oncology Branch, National Cancer Institute, National Institutes of Health, Bethesda, MD, USA

SOURCE: Antimicrobial Agents and Chemotherapy (1998), 42(11), 2898-2905
CODEN: AMACCQ; ISSN: 0066-4804

PUBLISHER: American Society for Microbiology

DOCUMENT TYPE: Journal

LANGUAGE: English

AB LY303366 is a novel semisynthetic deriv. of echinocandin B and a potent inhibitor of fungal (1,3)-.beta.-D-glucan synthase. The antifungal efficacy and safety of LY303366 were investigated in treatment and prophylaxis of primary pulmonary aspergillosis due to Aspergillus fumigatus in persistently neutropenic rabbits. Treatment study groups were either not treated (controls) or treated with amphotericin B (AmB) at 1 mg/kg of body wt. per day or with LY303366 at 1, 5, 10, and 20 mg/kg/day. In rabbits treated with LY303366, there was a significant improvement in survival and a redn. in organism-mediated pulmonary injury measured by the no. of infarcts, total lung wt., and ultrafast computerized tomog. scan pulmonary lesion score. Rabbits receiving prophylactic LY303366 also demonstrated significant improvement in survival and redn. in organism-mediated pulmonary injury. AmB and LY303366 had comparable therapeutic efficacies by all parameters with the exception of redn. in tissue burden of A. fumigatus, where AmB was superior to LY303366. LY303366 demonstrated a dose-dependent effect on hyphal injury with progressive truncation, swelling, and vacuolization. LY303366 administered in single doses of 1, 5, 10, and 20 mg/kg demonstrated dose-proportional increases in the max. concn. of drug in plasma and the area under the concn.-time curve from 0 to 72 h with no changes in plasma drug clearance. The 1-mg/kg dosage maintained plasma drug levels above the MIC for 18 h, and dosages of .gtoreq.5 mg/kg maintained plasma drug levels above the MIC for the entire 24-h dosing interval. There was no significant elevation of the concns. of hepatic transaminases or creatinine in serum in LY303366-treated rabbits. In summary, LY303366 improved survival and decreased pulmonary injury with no apparent toxicity in the treatment and prevention of invasive pulmonary aspergillosis in persistently neutropenic rabbits.

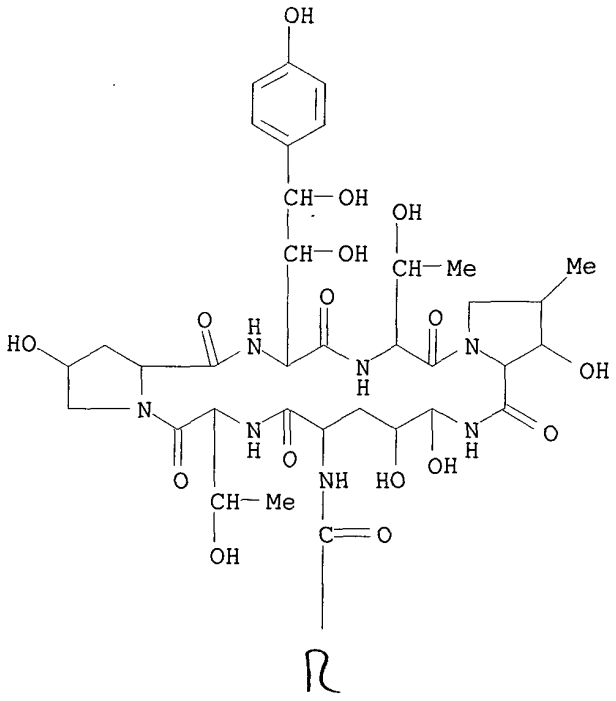
IT **166663-25-8**, LY303366
RL: ADV (Adverse effect, including toxicity); BAC (Biological activity or effector, except adverse); BPR (Biological process); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)
(antifungal efficacy, safety, and single-dose pharmacokinetics of LY303366, a novel echinocandin B, in exptl. pulmonary aspergillosis in persistently neutropenic rabbits)

RN 166663-25-8 HCAPLUS

CN Echinocandin B, 1-[(4R,5R)-4,5-dihydroxy-N2-[[4''-

(pentyloxy)[1,1':4',1''-terphenyl]-4-yl]carbonyl]-L-ornithine]-
(9CI) (CA INDEX NAME)

PAGE 1-A



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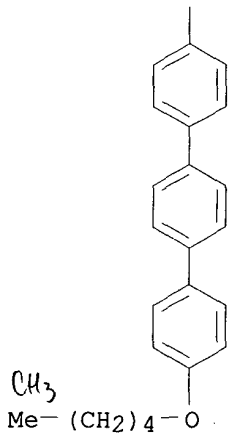
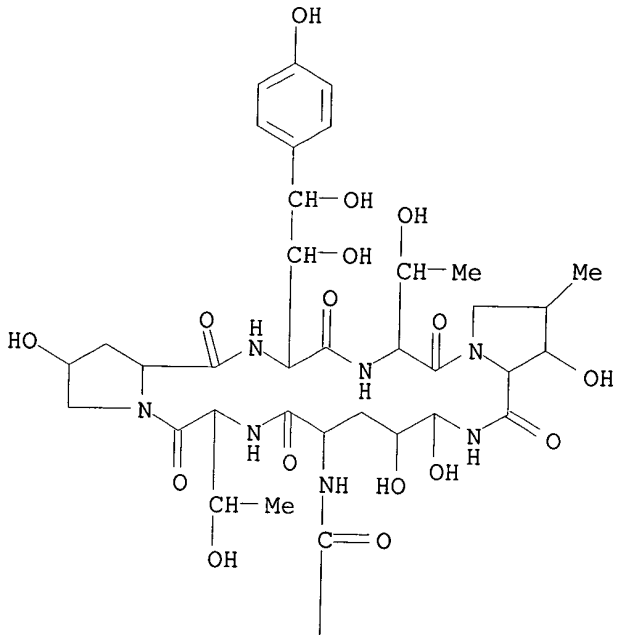


REFERENCE COUNT: 30 THERE ARE 30 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L31 ANSWER 2 OF 23 HCAPLUS COPYRIGHT 2003 ACS

ACCESSION NUMBER: 1998:683626 HCAPLUS
DOCUMENT NUMBER: 130:63531
TITLE: Activity of MK-0991 (L-743,872), a new echinocandin, compared with those of LY303366 and four other antifungal agents tested against blood stream isolates of Candida spp.
AUTHOR(S): Marco, F.; Pfaller, M. A.; Messer, S. A.; Jones, R. N.
CORPORATE SOURCE: Department of Pathology, University of Iowa College of Medicine, Iowa City, IA, 52242, USA
SOURCE: Diagnostic Microbiology and Infectious Disease (1998), 32(1), 33-37
CODEN: DMIDDZ; ISSN: 0732-8893
PUBLISHER: Elsevier Science Inc.
DOCUMENT TYPE: Journal
LANGUAGE: English
AB MK-0991 (formerly L-743,872) is a water sol. semisynthetic echinocandin that possess potent, broad-spectrum antifungal activity. We evaluated the in vitro activity of MK-0991 and an echinocandin deriv. LY303366, compared with that of itraconazole, fluconazole, amphotericin B and 5-flucytosine against 400 blood stream isolates of Candida spp. (nine species) obtained from more than 30 different medical centers. MICs for all antifungal drugs were detd. by the NCCLS method using RPMI 1640 test medium. Both MK-0991 and LY303366 were very active against all Candida spp. isolates (MIC90, 0.25 and 1 .mu.g/mL, resp.). MK-0991 was two-fold to 256-fold more active than amphotericin B, fluconazole, itraconazole (except against C. parapsilosis), and 5-flucytosine (except against C. glabrata and C. parapsilosis). LY303366 was comparable to MK-0991, but was fourfold less active against C. tropicalis (MIC90, 0.5 vs. 0.12 .mu.g/mL) and C. parapsilosis (MIC90, >2 vs. 1 .mu.g/mL). All of the isolates for which fluconazole and itraconazole had elevated MICs (.gtoreq.64 .mu.g/mL and .gtoreq.1 .mu.g/mL, resp.) were inhibited by .ltoreq.0.5 .mu.g/mL of MK-0991 and LY303366. These results suggest both MK-0991 and LY303366 possess promising antifungal activity and further in vitro and in vivo investigations are warranted.
IT **166663-25-8**, LY303366
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(comparison of the activity of the new echinocandin MK-0991 with those of LY303366 and four other antifungal agents against blood stream isolates of Candida spp.)
RN 166663-25-8 HCAPLUS
CN Echinocandin B, 1-[(4R,5R)-4,5-dihydroxy-N2-[[4''-(pentyloxy)[1,1':4',1''-terphenyl]-4-yl]carbonyl]-L-ornithine]- (9CI) (CA INDEX NAME)

PAGE 1-A



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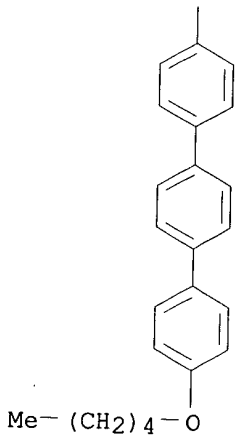


REFERENCE COUNT: 17 THERE ARE 17 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L31 ANSWER 3 OF 23 HCAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 1998:665023 HCAPLUS
DOCUMENT NUMBER: 130:12306
TITLE: In vitro activity of the echinocandin antifungal

Searcher : Shears 308-4994

agent LY303,366 in comparison with itraconazole and amphotericin B against Aspergillus spp.

AUTHOR(S): Oakley, Karen L.; Moore, Caroline B.; Denning, David W.

CORPORATE SOURCE: Department of Medicine, Hope Hospital, Manchester, UK

SOURCE: Antimicrobial Agents and Chemotherapy (1998), 42(10), 2726-2730
CODEN: AMACCQ; ISSN: 0066-4804

PUBLISHER: American Society for Microbiology

DOCUMENT TYPE: Journal

LANGUAGE: English

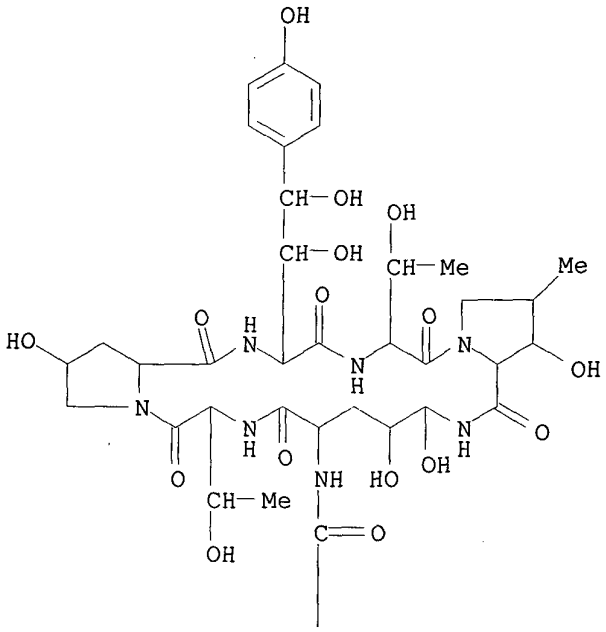
AB LY303,366 (LY) is a novel deriv. of the echinocandin class of antifungal agents. The in vitro activities of LY, itraconazole (ITZ), and amphotericin B (AMB) were assessed against 60 Aspergillus isolates, including 35 isolates of A. fumigatus, eight isolates of A. terreus, eight isolates of A. flavus, eight isolates of A. niger and one isolate of A. nidulans. Four A. fumigatus isolates were resistant to ITZ. Susceptibility testing for all drugs was performed with a broth microdilution procedure. LY was tested in two media: antibiotic medium 3 (AM3) and Casitone with 2% glucose (CAS) with an inoculum of 2 .times. 103 spores/mL. ITZ and AMB were tested in RPMI 1640 with 2% glucose with an inoculum of 1 .times. 106 spores/mL. All tests were incubated at 37.degree.C for 48 h. A novel end point was used to det. a minimal effective concn. (MEC) for LY, i.e., almost complete inhibition of growth save a few tiny spherical colonies attached to the microplate. MICs were measured for ITZ and AMB with a no-growth end point. Ranges and geometric mean (GM) MECs were from 0.0018 to >0.5 and 0.0039 mg/L and from 0.0018 to >0.5 and 0.008 mg/L for LY in AM3 and LY in CAS, resp. Differences between species were apparent, with A. flavus being significantly less susceptible to LY than any other species tested with both media (P .ltoreq. 0.05). Ranges and GM MICs were from 0.125 to >16 and 0.7 mg/L for ITZ and from 0.25 to 16 and 1.78 mg/L for AMB. Minimal fungicidal concns. (MFCs) were also detd. for all drugs. GM MFCs were 0.018, 0.09, 19.76, and 12.64 mg/L for LY in AM3, LY in CAS, ITZ, and AMB, resp. LY in AM3 and LY in CAS were fungicidal for 86.7 and 68% of isolates, resp. (98% killing). In comparison, ITZ and AMB were fungicidal for 35 and 70% of isolates, resp. (99.99% killing). A reproducibility study was performed on 20% of the isolates. For 12 isolates retested, the MEC or MIC was the same or was within 1 diln. of the original value for 11, 11, 10, and 9 isolates for LY in AM3, LY in CAS, ITZ, and AMB, resp. In conclusion, LY seems to be a promising antifungal agent with excellent in vitro activity against Aspergillus spp.

IT **166663-25-8**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(in vitro activity of the echinocandin antifungal agent LY303,366 in comparison with itraconazole and amphotericin B against Aspergillus spp.)

RN 166663-25-8 HCAPLUS

CN Echinocandin B, 1-[(4R,5R)-4,5-dihydroxy-N2-[[4''-(pentyloxy)[1,1':4',1''-terphenyl]-4-yl]carbonyl]-L-ornithine]- (9CI) (CA INDEX NAME)

PAGE 1-A



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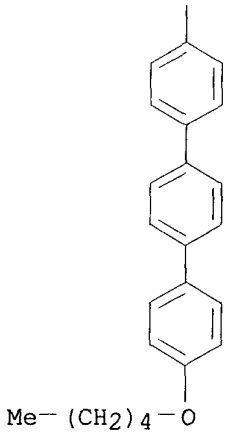

REFERENCE COUNT: 12 THERE ARE 12 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L31 ANSWER 4 OF 23 HCAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 1998:633639 HCAPLUS
DOCUMENT NUMBER: 130:22724
TITLE: Comparison of in vitro activities of the new triazole SCH56592 and the echinocandins MK-0991

Searcher : Shears 308-4994

(L-743,872) and LY303366 against opportunistic filamentous and dimorphic fungi and yeasts

AUTHOR(S): Espinel-Ingroff, Ana
CORPORATE SOURCE: Division of Infectious Diseases, Medical College of Virginia, Virginia Commonwealth University, Richmond, VA, 23298-0049, USA

SOURCE: Journal of Clinical Microbiology (1998), 36(10), 2950-2956
CODEN: JCMIDW; ISSN: 0095-1137
PUBLISHER: American Society for Microbiology
DOCUMENT TYPE: Journal
LANGUAGE: English

AB The in vitro antifungal activities of SCH56592, MK-0991, and LY303366 against 83 isolates of Acremonium strictum, Aspergillus flavus, Aspergillus fumigatus, Aspergillus terreus, Bipolaris spp., Blastomyces dermatitidis, Cladophialophora bantiana, Fusarium oxysporum, Fusarium solani, Histoplasma capsulatum, Phialophora spp., Pseudallescheria boydii, Rhizopus arrhizus, Scedosporium prolificans, and Sporothrix schenckii were compared. The in vitro activities of these agents against 104 isolates of yeast pathogens of Candida spp., Cryptococcus neoformans, and Trichosporon beigelii were also compared. MICs were detd. by following a procedure under evaluation by the National Committee for Clin. Lab. Stds. (NCCLS) for broth microdilution testing of the filamentous fungi (visual MICs) and the NCCLS M27-A broth microdilution method for yeasts (both visual and turbidimetric MICs). The in vitro fungicidal activity of SCH56592 was superior (min. fungicidal concns. [MFCs], 0.25 to 4 .mu.g/mL for 7 of 18 species tested) to those of MK-0991 and LY303366 (MFCs, 8 to >16 .mu.g/mL for all species tested) for the molds tested, but the echinocandins had a broader spectrum of fungicidal activity (MFCs at which 90% of strains are inhibited [MFC90s], 0.5 to 4 .mu.g/mL for 6 of 9 species tested) than SCH56592 (MFC90s, 0.25 to 8 .mu.g/mL for 4 of 9 species tested) against most of the yeasts tested. Neither echinocandin had in vitro activity (MICs, >16 .mu.g/mL) against C. neoformans and T. beigelii, while the SCH56592 MICs ranged from 0.12 to 1.0 .mu.g/mL for these two species. The MICs of the three agents for the other species ranged from <0.03 to 4 .mu.g/mL. These results suggest that these new agents have broad-spectrum activities in vitro; their effectiveness in the treatment of human mycoses is to be detd.

IT **166663-25-8**, LY303366
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(comparison of in vitro activities of the new triazole SCH56592 and the echinocandins MK-0991 and LY303366 against opportunistic filamentous and dimorphic fungi and yeasts)

RN 166663-25-8 HCAPLUS
CN Echinocandin B, 1-[(4R,5R)-4,5-dihydroxy-N2-[[4''-(pentyloxy)[1,1':4',1''-terphenyl]-4-yl]carbonyl]-L-ornithine]- (9CI) (CA INDEX NAME)

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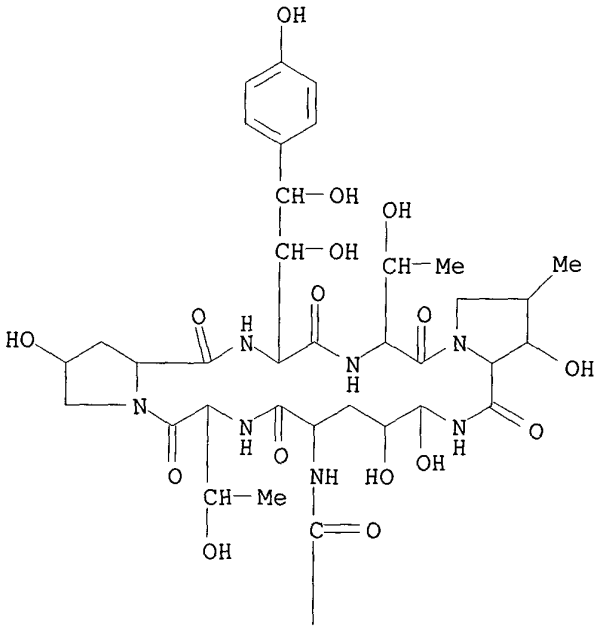

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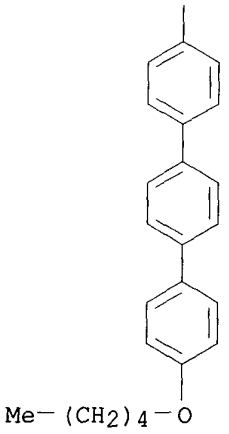


REFERENCE COUNT: 33 THERE ARE 33 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L31 ANSWER 5 OF 23 HCAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 1998:601957 HCAPLUS
DOCUMENT NUMBER: 129:300016
TITLE: Susceptibilities of Candida species isolated

Searcher : Shears 308-4994

from the lower gastrointestinal tracts of high-risk patients to the new semisynthetic echinocandin LY303366 and other antifungal agents

AUTHOR(S): Zhanel, George G.; Karlowsky, James A.; Zelenitsky, Sheryl A.; Turik, Michael A.; Hoban, Daryl J.

CORPORATE SOURCE: Department of Medical Microbiology, Health Sciences Centre, Winnipeg, MB, R3A 1R9, Can.

SOURCE: Antimicrobial Agents and Chemotherapy (1998), 42(9), 2446-2448
CODEN: AMACCQ; ISSN: 0066-4804

PUBLISHER: American Society for Microbiology

DOCUMENT TYPE: Journal

LANGUAGE: English

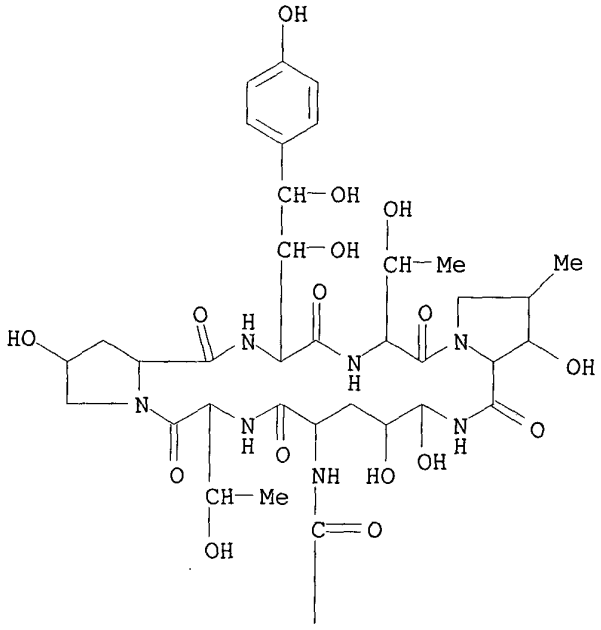
AB Fifty-two percent of stool specimens collected from 1,200 high-risk patients were colonized with yeasts, primarily Candida albicans (53.6%) and Candida glabrata (35.7%). Susceptibilities to all antifungal agents tested, including LY303366, were similar to those reported previously for Candida species isolated from blood.

IT **166663-25-8**, LY303366
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(susceptibilities of Candida species isolated from the lower gastrointestinal tracts of high-risk patients to the new semisynthetic echinocandin LY303366 and other antifungal agents)

RN 166663-25-8 HCAPLUS

CN Echinocandin B, 1-[(4R,5R)-4,5-dihydroxy-N2-[[4''-(pentyloxy)[1,1':4',1''-terphenyl]-4-yl]carbonyl]-L-ornithine]-(9CI) (CA INDEX NAME)

PAGE 1-A



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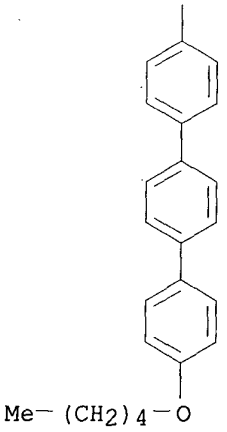

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L31 ANSWER 6 OF 23 HCAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 1998:520488 HCAPLUS
DOCUMENT NUMBER: 129:276286
TITLE: Studies on the phosphorylation of LY303366

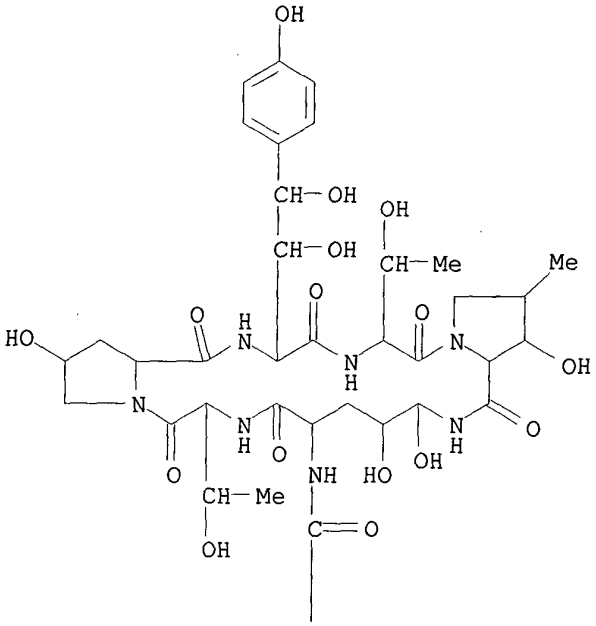
Searcher : Shears 308-4994

AUTHOR(S): Udodong, Uko E.; Turner, William W.; Astelford, Bret A.; Brown, Frank, Jr.; Clayton, Marcella T.; Dunlap, Steven E.; Frank, Scott A.; Grutsch, John L.; LaGrandeur, Lisa M.; Verral, Daniel E.; Werner, John A.
CORPORATE SOURCE: Lilly Research Laboratories, Lilly Corporate Center, Indianapolis, IN, 46285, USA
SOURCE: Tetrahedron Letters (1998), 39(34), 6115-6118
CODEN: TELEAY; ISSN: 0040-4039
PUBLISHER: Elsevier Science Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 129:276286
GI

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

AB Phosphorylation of LY303366 was studied in THF and DMF. Benzyl phosphate (I) could be prepd. in excellent yield using LiOH as the base. Both I and the derived phosphonic acid monosodium salt were prone to undergo hydrolytic dephosphorylation.
IT **166663-25-8**, LY 303366
RL: RCT (Reactant); RACT (Reactant or reagent)
(studies on the phosphorylation of LY303366)
RN 166663-25-8 HCAPLUS
CN Echinocandin B, 1-[(4R,5R)-4,5-dihydroxy-N2-[[4''-(pentyloxy)[1,1':4',1''-terphenyl]-4-yl]carbonyl]-L-ornithine]-(9CI) (CA INDEX NAME)

PAGE 1-A



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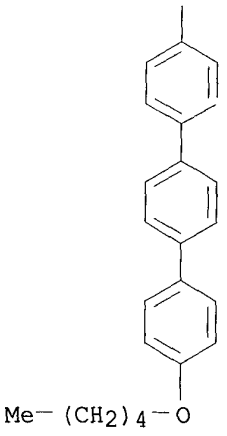

REFERENCE COUNT: 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L31 ANSWER 7 OF 23 HCAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 1998:292085 HCAPLUS
DOCUMENT NUMBER: 129:79003
TITLE: In vitro activity of two echinocandin

Searcher : Shears 308-4994

derivatives, LY303366 and MK-0991 (L-743,792), against clinical isolates of Aspergillus, Fusarium, Rhizopus, and other filamentous fungi

AUTHOR(S): Pfaller, M. A.; Marco, F.; Messer, S. A.; Jones, R. N.

CORPORATE SOURCE: Medical Microbiology Division, Department of Pathology, University of Iowa College of Medicine, Iowa City, IA, 52242, USA

SOURCE: Diagnostic Microbiology and Infectious Disease (1998), 30(4), 251-255
CODEN: DMIDDZ; ISSN: 0732-8893

PUBLISHER: Elsevier Science Inc.

DOCUMENT TYPE: Journal

LANGUAGE: English

AB LY303366 and MK-0991 (previously L-743,792) are new echinocandin derivs. with excellent broad-spectrum antifungal activity. The authors investigated the in vitro activity of LY303366, MK-0991, itraconazole, amphotericin B, and 5-flucytosine against 51 clin. isolates of filamentous fungi, including Aspergillus flavus (10), A. fumigatus (12), Fusarium spp. (13), Rhizopus spp. (6), Pseudallescheria boydii (5), and one isolate each of Acremonium spp., A. niger, A. terreus, Paecilomyces spp., and Trichoderma spp. In vitro susceptibility testing was performed using a microdilution broth method performed according to National Committee for Clin. Lab. Stds. guidelines. LY303366 was two- to fourfold more active than MK-0991 against A. flavus, A. fumigatus, and Trichoderma spp. Both LY303366 and MK-0991 were considerably more active (MIC90 of 0.03-0.12 .mu.g/mL) than itraconazole, amphotericin B, and 5-flucytosine against Aspergillus spp., but were less active than itraconazole and amphotericin B against Rhizopus spp. MK-0991 was more active than either LY303366 or itraconazole against Acremonium spp., Paecilomyces spp., and P. boydii. These data demonstrate promising activity of both LY303366 and MK-0991 against Aspergillus spp. and other species of filamentous fungi that are likely to be encountered clin. Further in vitro and in vivo investigation is indicated.

IT **166663-25-8**, LY303366
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)
(in vitro antifungal activity of two echinocandin derivs.)

RN 166663-25-8 HCAPLUS

CN Echinocandin B, 1-[(4R,5R)-4,5-dihydroxy-N2-[[4''-(pentyloxy)[1,1':4',1''-terphenyl]-4-yl]carbonyl]-L-ornithine]- (9CI) (CA INDEX NAME)

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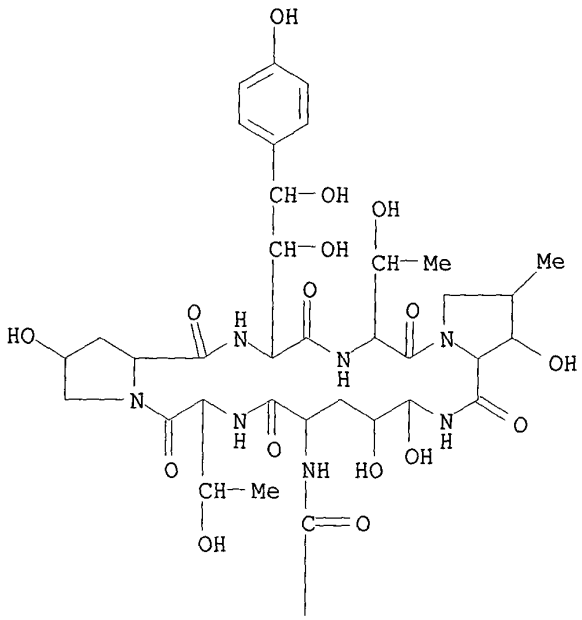

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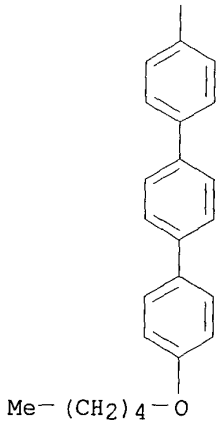

REFERENCE COUNT: 19 THERE ARE 19 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L31 ANSWER 8 OF 23 HCAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 1998:271687 HCAPLUS
DOCUMENT NUMBER: 129:38307
TITLE: Influence of test conditions on antifungal

Searcher : Shears 308-4994

time-kill curve results: proposal for standardized methods

AUTHOR(S): Klepser, Michael E.; Ernst, Erika J.; Lewis, Russell E.; Ernst, Michael E.; Pfaller, Michael A.

CORPORATE SOURCE: College of Pharmacy, The University of Iowa, Iowa City, IA, 52242, USA

SOURCE: Antimicrobial Agents and Chemotherapy (1998), 42(5), 1207-1212
CODEN: AMACCQ; ISSN: 0066-4804

PUBLISHER: American Society for Microbiology

DOCUMENT TYPE: Journal

LANGUAGE: English

AB This study was designed to examine the effects of antifungal carryover, agitation, and starting inoculum on the results of time-kill tests conducted with various Candida species. Two isolates each of Candida albicans, Candida tropicalis, and Candida glabrata were utilized. Test antifungal agents included fluconazole, amphotericin B, and LY303366. Time-kill tests were conducted in RPMI 1640 medium buffered with morpholinepropanesulfonic acid (MOPS) to a pH of 7.0 and incubated at 35.degree.C. Prior to testing, the existence of antifungal carryover was evaluated at antifungal concns. ranging from 1.times. to 16.times. MIC by four plating methods: direct plating of 10, 30, and 100 .mu.l of test suspension and filtration of 30 .mu.l of test suspension through a 0.45-.mu.m-pore-size filter. Time-kill curves were performed with each isolate at drug concns. equal to 2.times. MIC, using a starting inoculum of approx. 105 CFU/mL, and incubated with or without agitation. Last, inoculum expts. were conducted over three ranges of starting inocula: 5 .times. 102 to 1 .times. 104, >1 .times. 104 to 1 .times. 106, and >1 .times. 106 to 1 .times. 108 CFU/mL. Significant antifungal carryover (>25% redn. in CFU/mL from the control value) was obsd. with amphotericin B and fluconazole; however, carryover was eliminated with filtration. Agitation did not appreciably affect results. The starting inoculum did not significantly affect the activity of fluconazole or amphotericin B; however, the activity of LY303366 may be influenced by the starting inoculum. Before antifungal time-kill curve methods are routinely employed by investigators, methodol. should be scrutinized and standardized procedures should be developed.

IT **166663-25-8**, LY303366.
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)
(influence of test conditions on antifungal time-kill curve results and proposal for standardized methods)

RN 166663-25-8 HCAPLUS

CN Echinocandin B, 1-[(4R,5R)-4,5-dihydroxy-N2-[[4''-(pentyloxy)[1,1':4',1''-terphenyl]-4-yl]carbonyl]-L-ornithine]-(9CI) (CA INDEX NAME)

Audet
09/942435


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     FILE 'REGISTRY' ENTERED AT 14:46:58 ON 06 JUN 2003
                 E ECHINOCANDIN/CN 5
L1             1 S E3
                 E FRUCTOSE/CN 5
L2             2 S E3
L3             1 S 183211-59-8/RN
L4             2 S L1 OR L3

L4   ANSWER 1 OF 2  REGISTRY  COPYRIGHT 2003 ACS
RN   183211-59-8  REGISTRY
CN   Cilofungin, 1-[(4R,5R)-N2-[(4''-butoxy[1,1':4',1''-terphenyl]-4-
     yl)carbonyl]-4,5-dihydroxy-L-ornithine]- (9CI)  (CA INDEX NAME)
OTHER CA INDEX NAMES:
CN   Echinocandin B, 1-[N2-[(4''-butoxy[1,1':4',1''-terphenyl]-4-
     yl)carbonyl]-(4R,5R)-4,5-dihydroxy-L-ornithine]-
FS   PROTEIN SEQUENCE; STEREOSEARCH
MF   C57 H71 N7 O17
SR   CA
LC   STN Files:   CA, CAPLUS, TOXCENTER, USPATFULL

**RELATED SEQUENCES AVAILABLE WITH SEQLINK**
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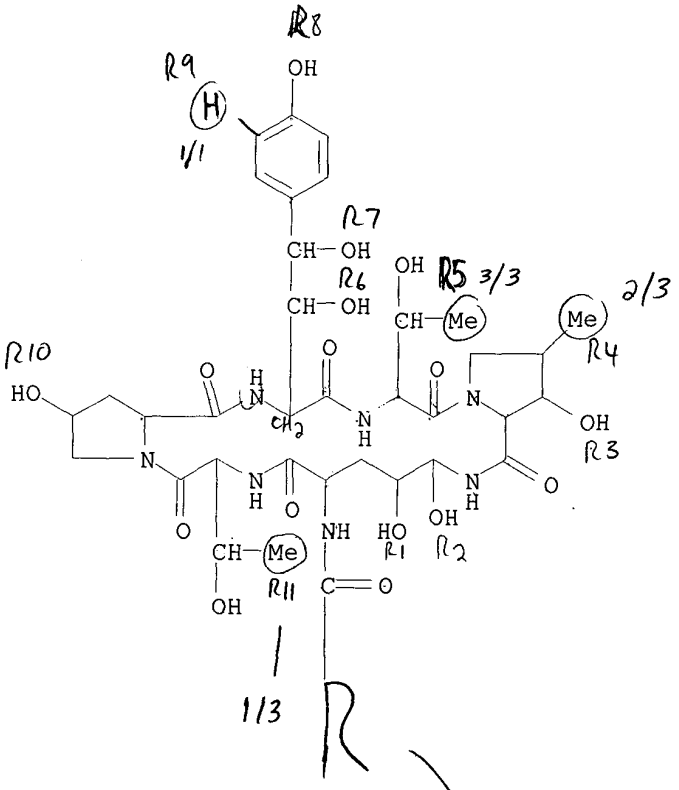
-key terms

DN in APPL's



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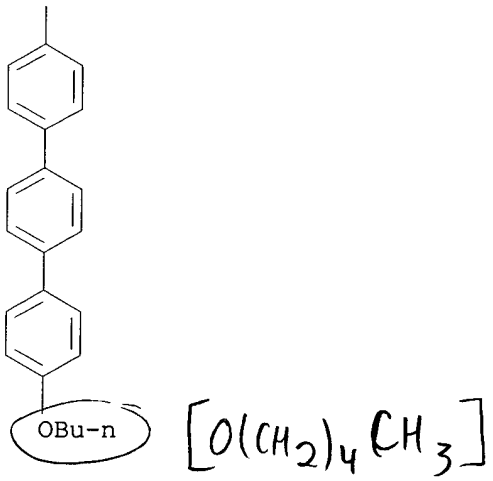
Searcher : Shears 308-4994



5 REFERENCES IN FILE CA (1957 TO DATE)
1 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
5 REFERENCES IN FILE CAPLUS (1957 TO DATE)

REFERENCE 1: 136:341005

REFERENCE 2: 133:227789

REFERENCE 3: 133:227787

REFERENCE 4: 126:75252

REFERENCE 5: 125:329474

L4 ANSWER 2 OF 2 REGISTRY COPYRIGHT 2003 ACS
RN [redacted] REGISTRY
CN **Echinocandin (9CI)** (CA INDEX NAME)
MF Unspecified
CI MAN
LC STN Files: ADISNEWS, AGRICOLA, BIOBUSINESS, BIOSIS, BIOTECHNO, CA, CAPLUS, CIN, EMBASE, NAPRALERT, PROMT, TOXCENTER, USPATFULL

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***
48 REFERENCES IN FILE CA (1957 TO DATE)
15 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
48 REFERENCES IN FILE CAPLUS (1957 TO DATE)

REFERENCE 1: 138:317192

REFERENCE 2: 138:147058

REFERENCE 3: 138:95591

REFERENCE 4: 138:78490

REFERENCE 5: 138:69760

REFERENCE 6: 138:39464

REFERENCE 7: 137:165862

REFERENCE 8: 137:106402

REFERENCE 9: 137:59948

REFERENCE 10: 137:68

FILE 'HCAPLUS' ENTERED AT 14:49:07 ON 06 JUN 2003
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L3 1 SEA FILE=REGISTRY ABB=ON PLU=ON 183211-59-8/RN
L4 2 SEA FILE=REGISTRY ABB=ON PLU=ON L1 OR L3
L5 356 SEA FILE=HCAPLUS ABB=ON PLU=ON L4 OR ECHINOCANDIN
L6 5 SEA FILE=HCAPLUS ABB=ON PLU=ON L5 AND (GRANUL? OR POWDER?)

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L1 1 SEA FILE=REGISTRY ABB=ON PLU=ON ECHINOCANDIN/CN
L2 2 SEA FILE=REGISTRY ABB=ON PLU=ON FRUCTOSE/CN
L3 1 SEA FILE=REGISTRY ABB=ON PLU=ON 183211-59-8/RN
L4 2 SEA FILE=REGISTRY ABB=ON PLU=ON L1 OR L3
L5 356 SEA FILE=HCAPLUS ABB=ON PLU=ON L4 OR ECHINOCANDIN
L7 3 SEA FILE=HCAPLUS ABB=ON PLU=ON L5 AND (L2 OR FRUCTOSE)

=> s l6 or l7
L8 7 L6 OR L7

L8 ANSWER 1 OF 7 HCAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 2003:23348 HCAPLUS
DOCUMENT NUMBER: 138:95591
TITLE: Adhesive treatment for oral fungal infection
INVENTOR(S): Narang, Upvan
PATENT ASSIGNEE(S): Closure Medical Corporation, USA
SOURCE: U.S. Pat. Appl. Publ., 10 pp.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2003007947	A1	20030109	US 2001-898092	20010705

PRIORITY APPLN. INFO.: US 2001-898092 20010705

AB A method of treating or preventing oral fungal infection includes applying a polymerizable monomer adhesive compn. to an area afflicted with or susceptible to oral fungal infection, optionally with at least one of an addnl. anti-fungal agent, and allowing the polymerizable monomer compn. to polymerize to form a polymer film over the area.

IT **80619-41-6, Echinocandin**
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(adhesive treatment for oral fungal infection)

L8 ANSWER 2 OF 7 HCAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 2003:23347 HCAPLUS

DOCUMENT NUMBER: 138:78490
TITLE: Adhesive treatment for tinea cruris
INVENTOR(S): Narang, Upvan; Nicholson, William S. C.; Sherbondy, Anthony; Szabo, Gabriel N.
PATENT ASSIGNEE(S): Closure Medical Corporation, USA
SOURCE: U.S. Pat. Appl. Publ., 10 pp.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2003007946	A1	20030109	US 2001-898005	20010705

PRIORITY APPLN. INFO.: US 2001-898005 20010705

AB A method of treating or preventing tinea cruris, commonly known as Jock itch, includes applying a polymerizable monomer adhesive compn. to an area of skin afflicted with or susceptible to tinea cruris, optionally with at least 1 of an addnl. antifungal agent or a skin care additive, and allowing the polymerizable monomer compn. to polymerize to form a polymer film over the area of skin. A 2-octyl cyanoacrylate monomer compn. is prepd. by adding 30 mg haloprogin to 2 mL 2-octyl cyanoacrylate. The mixt. is sealed in a glass vial and stirred. The characteristics of the compn. are obsd. at about 1 min after prepn. and later at least 24 h after prepn. The soln. remains clear, indicating that haloprogin is sol. in the monomer and does not cause premature polymn. The compn. is then applied to an affected area of skin showing the characteristics of tinea cruris. The monomer compn. polymerizes in under 1 min, resulting in a polymd. film of material covering the affected area. The polymd. film will remain in place for at least three days.

IT **80619-41-6, Echinocandin**
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(antifungal agent; adhesive treatment for tinea cruris)

L8 ANSWER 3 OF 7 HCAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 2001:545525 HCAPLUS
DOCUMENT NUMBER: 135:157672
TITLE: Cyclic peptide compositions for nasal administration
INVENTOR(S): Horii, Ikuo; Kobayashi, Kazuko; Shimma, Nobuo; Yanagawa, Akira
PATENT ASSIGNEE(S): Basilea Pharmaceutica A.-G., Switz.
SOURCE: PCT Int. Appl., 117 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001052894	A2	20010726	WO 2001-EP163	20010109
WO 2001052894	A3	20020131		

W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV,

MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

EP 1251827 A2 20021030 EP 2001-909587 20010109
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR
BR 2001007764 A 20021112 BR 2001-7764 20010109
US 2001038824 A1 20011108 US 2001-765846 20010119
PRIORITY APPLN. INFO.: EP 2000-101057 A 20000120
WO 2001-EP163 W 20010109

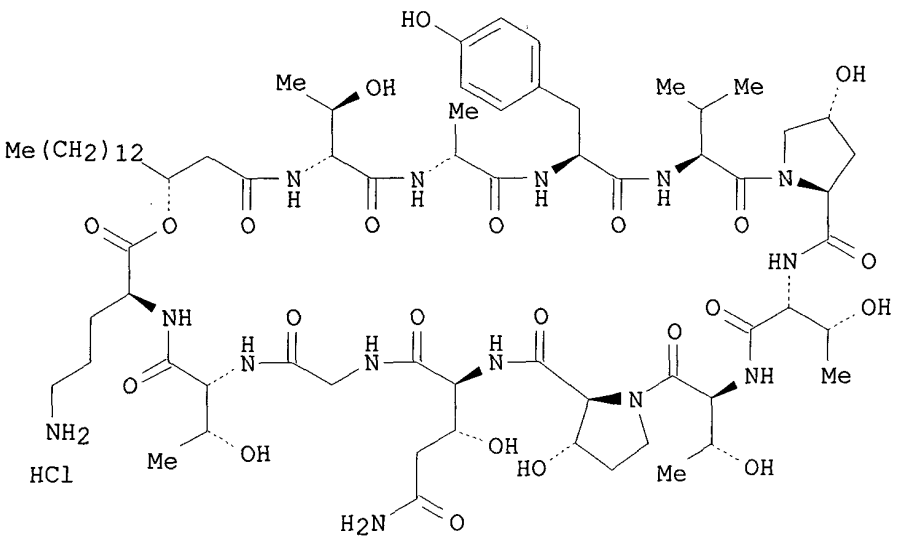
OTHER SOURCE(S): MARPAT 135:157672

AB The present invention relates to a nasal compn. of physiol. active cyclic peptides and salts that are prepd. by homogeneously dispersing an active cyclic peptide such as antifungal cyclic peptides (aerothricin, **echinocandin** analogs, pneumocandin analogs, and aureobasidin), antibacterial cyclic peptides (e.g., vancomycin, daptomycin), cyclosporin A, lanreotide, vapreotide, vasopressin antagonist and eptifibatide in a unique carrier. The **powdery** or cryst. carrier contains a water insol. polyvalent metal carrier, or org. carrier having a mean particle size of 20-500 .mu.m, in the presence or absence of an absorption enhancer and by homogeneously adsorbing onto the carrier, and its use for therapeutic treatment of disease such as systemic fungal infections by intranasal administration. The compn. can be nasally administered in a **powder** form. Thus, 201 mg Aerothricin 133 and 599 mg CaCO3 (mean particle size: 40-60 .mu.m) were mixed well. Then, 200 .mu.L water was added, and mixing was continued until the mixt. became a paste and the resulting pasty solid was freeze-dried at -50.degree., and further dried at 300.degree. for 3 h in vacuo. After large particles in the dry **powder** were broken into small particles, 8 mg of calcium stearate was added and the mixt. was passed through 180-.mu.m-mesh. Aerothricin 133 was synthesized by a series of steps.

IT **80619-41-6D, Echinocandin**, analogs
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(prepn. of cyclic peptide compns. for nasal administration)

L8 ANSWER 4 OF 7 HCAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 2000:702493 HCAPLUS
DOCUMENT NUMBER: 133:360662
TITLE: FR901469, a novel antifungal antibiotic from an unidentified fungus No.11243. I. Taxonomy, fermentation, isolation, physico-chemical properties and biological properties
AUTHOR(S): Fujie, Akihiko; Iwamoto, Toshiro; Muramatsu, Hideyuki; Okudaira, Terumi; Nitta, Kumiko; Nakanishi, Tomoko; Sakamoto, Kazutoshi; Hori, Yasuhiro; Hino, Motohiro; Hashimoto, Seiji; Okuhara, Masakuni
CORPORATE SOURCE: Exploratory Research Laboratories, Fujisawa Pharmaceutical Co., Ltd., Tsukuba, 300-2698, Japan
SOURCE: Journal of Antibiotics (2000), 53(9), 912-919
CODEN: JANTAJ; ISSN: 0021-8820

PUBLISHER: Japan Antibiotics Research Association
DOCUMENT TYPE: Journal
LANGUAGE: English
GI



I

AB FR901469 (I) is a novel antifungal antibiotic produced by an unidentified fungus, No.11243. This compd. was isolated from the culture broth by solvent extn., HP-20 and YMC ODS gel column chromatog., and lyophilization. FR901469 is a white **powder** which melts at 182.apprx.187.degree.C and possesses the mol. formula C71H116N14O23. This compd. has good water soly. FR901469 inhibited the activity of 1,3-.beta.-glucan synthase from Candida albicans with an IC50 value of 0.05 .mu.g/mL, and displayed greater inhibitory activity than other 1,3-.beta.-glucan synthase inhibitors, such as WF11899A, **echinocandin** B, aculeacin A, and papulacandin B.

REFERENCE COUNT: 19 THERE ARE 19 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 5 OF 7 HCAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 2000:628163 HCAPLUS
DOCUMENT NUMBER: 133:222965
TITLE: Preparation of **echinocandin** /carbohydrate complexes as fungicides
INVENTOR(S): Barrew, Larry Arnold; Milton, Nathaniel; Sabatowski, James Lawrence; Moder, Kenneth Philip
PATENT ASSIGNEE(S): Eli Lilly and Co., USA
SOURCE: PCT Int. Appl., 35 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English

Searcher : Shears 308-4994

Pos. DP w/ Prov. Filed Same day.

L4

Call up

inventor search or all

FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000052037	A1	20000908	WO 2000-US5508	20000302
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, GM, HR, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
EP 1157030	A1	20011128	EP 2000-917703	20000302
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BR 2000008712	A	20011226	BR 2000-8712	20000302
JP 2002539090	T2	20021119	JP 2000-602261	20000302
US 2002160942	A1	20021031	US 2001-942458	20010829

PRIORITY APPLN. INFO.: US 1999-122692P P 19990303
WO 2000-US5508 W 20000302

OTHER SOURCE(S): MARPAT 133:222965
GI

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

AB A complex of an **echinocandin** compd. with a carbohydrates I (R = alkyl, alkenyl, alkynyl, heteroaryl; R1-R3,R6,R7,R10 = independently H, OH; R4 = H, Me, CH2CONH2; R5, R11 = independently Me, H; R8 = OH, OSO3H, OPO3H2, substituted phosphate; R9 = H, OH, OSO3H) were prepd. as fungicides and having improved thermal stability and water soly. Thus, I (R = Z, R1-R3, R6-R8, R10 = OH, R3 = R5 = R11 = Me; R9 = H) was prepd. and complexed with **fructose** and tested in vitro as antifungal agent.

REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

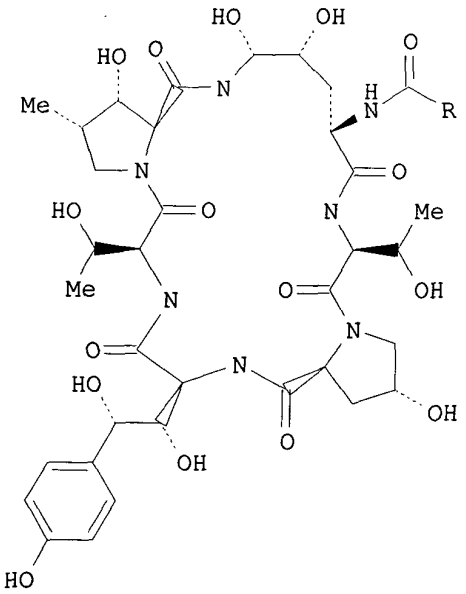
L8 ANSWER 6 OF 7 HCAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 2000:627958 HCAPLUS
DOCUMENT NUMBER: 133:227789
TITLE: Processes for making pharmaceutical oral **echinocandin** formulations and compositions
INVENTOR(S): [redacted]wier, John Richard; [redacted]aylor, Jerry
PATENT ASSIGNEE(S): Eli Lilly and Company, USA
SOURCE: PCT Int. Appl., 40 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

2 More

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000051567	A1	20000908	WO 2000-US5547	20000302
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, GM, HR, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
EP 1156784	A1	20011128	EP 2000-912160	20000302
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
BR 2000008713	A	20011226	BR 2000-8713	20000302
JP 2002538097	T2	20021112	JP 2000-602036	20000302
US 2002151474	A1	20021017	US 2001-942435	20010829
PRIORITY APPLN. INFO.:			US 1999-122693P P	19990303
			WO 2000-US5547 W	20000302

OTHER SOURCE(S): MARPAT 133:227789

GI



I

AB A fluid bed spray process is described where one or more carbohydrates are incorporated into an **echinocandin** formulation to provide a significant improvement in thermal stability. The carbohydrate is solubilized with an **echinocandin** compd. or **echinocandin**/carbohydrate complex in a solvent(s) to form a pharmaceutical soln. which is sprayed onto the surface of a **granular** diluent or carrier.

Alternatively, a **granulating** agent is added to the pharmaceutical soln. which is then sprayed onto the surface of a non-**granular** diluent or carrier. I was prepd., and a **fructose** complex with I also prepd.

IT **183211-59-8P**
RL: RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
(prepn. of **echinocandin** carbohydrate complexes for oral pharmaceuticals)

IT **57-48-7, Fructose,** biological studies
RL: RCT (Reactant); THU (Therapeutic use); BIOL (Biological study); RACT (Reactant or reagent); USES (Uses)
(prepn. of **echinocandin** carbohydrate complexes for oral pharmaceuticals)

IT **80619-41-6DP, Echinocandin,** derivs.
183211-59-8DP, complex with carbohydrates
RL: SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of **echinocandin** carbohydrate complexes for oral pharmaceuticals)

REFERENCE COUNT: 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 7 OF 7 HCAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 2000:627955 HCAPLUS
DOCUMENT NUMBER: 133:227787
TITLE: **Echinocandin** pharmaceutical formulations containing micelle-forming surfactants
INVENTOR(S): Milton, Nathaniel; Moder, Kenneth Philip; Sabatowski, James Lawrence; Sweetana, Stephanie Ann
PATENT ASSIGNEE(S): Eli Lilly and Company, USA
SOURCE: PCT Int. Appl., 44 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000051564	A1	20000908	WO 2000-US5546	20000302
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, EE, ES, FI, GB, GE, GH, GM, HR, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
BR 2000009249	A	20011120	BR 2000-9249	20000302
EP 1156782	A1	20011128	EP 2000-910391	20000302
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				

JP 2002538095 T2 20021112 JP 2000-602034 20000302
US 2003054981 A1 20030320 US 2001-942431 20010829
PRIORITY APPLN. INFO.: US 1999-122623P P 19990303
WO 2000-US5546 W 20000302
OTHER SOURCE(S): MARPAT 133:227787
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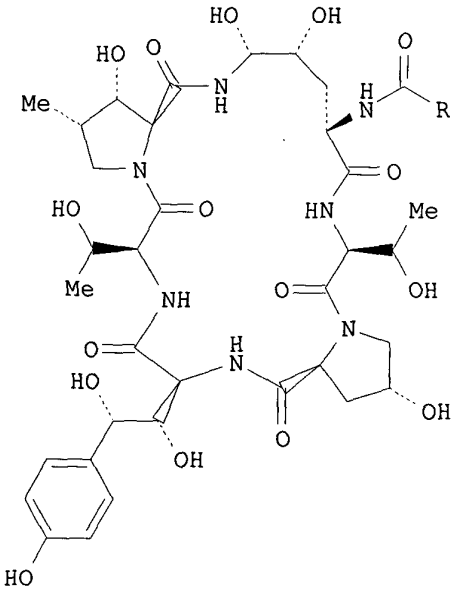


I

AB Pharmaceutical formulations are described comprising an **echinocandin** compd. or **echinocandin**/carbohydrate complex and a pharmaceutically acceptable micelle-forming surfactant in a non-toxic aq. solvent such that the solubilization of the **echinocandin** compd. is optimized and the ability to freeze-dry the soln. is maintained. Both the soln. and freeze-dried formulations have increased stability. A bulking agent, tonicity agent buffer and/or a stabilizing agent may optionally be added to the formulations to further enhance the stability of the formulation. I was prepd. and a freeze-dried prepn. was prepd. contg. I, mannitol and trehalose.

IT **57-48-7, Fructose,** biological studies
RL: MOA (Modifier or additive use); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(**echinocandin** pharmaceutical formulations contg. micelle-forming surfactants)

IT **183211-59-8P**
RL: SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(**echinocandin** pharmaceutical formulations contg. micelle-forming surfactants)

IT **80619-41-6, Echinocandin**
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(**echinocandin** pharmaceutical formulations contg. micelle-forming surfactants)
REFERENCE COUNT: 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

(FILE 'MEDLINE, BIOSIS, EMBASE, WPIDS, CONFSCI, SCISEARCH, JICST-EPLUS, JAPIO' ENTERED AT 14:50:56 ON 06 JUN 2003)
L9 45 S L6
L10 3 S L7
L11 47 S L9 OR L10
L12 38 DUP REM L11 (9 DUPLICATES REMOVED)

L12 ANSWER 1 OF 38 EMBASE COPYRIGHT 2003 ELSEVIER SCI. B.V.
ACCESSION NUMBER: 2003103352 EMBASE
TITLE: Management of infection in children with malignancy.
AUTHOR: Miflin G.; Kinsey S.E.
CORPORATE SOURCE: S.E. Kinsey, Department of Paediatric Haematology, Children's Day Hospital, St. James University Hospital, Beckett Street, Leeds LS9 7TF, United Kingdom. sally.kinsey@leeds.nhs.uk
SOURCE: European Journal of Cancer, (2003) 39/5 (644-651). Refs: 62
ISSN: 0959-8049 CODEN: EJCAEL
COUNTRY: United Kingdom
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 016 Cancer
036 Health Policy, Economics and Management
037 Drug Literature Index
038 Adverse Reactions Titles
039 Pharmacy
LANGUAGE: English

L12 ANSWER 2 OF 38 EMBASE COPYRIGHT 2003 ELSEVIER SCI. B.V.
ACCESSION NUMBER: 2003198323 EMBASE
TITLE: A new antifungal sterol sulfate, sch 601324, from Chrysosporium sp.
AUTHOR: Yang S.-W.; Buevich A.; Chan T.-M.; Terracciano J.; Chen G.; Loebenberg D.; Patel M.; Boehm E.; Gullo V.; Pramanik B.; Chu M.
CORPORATE SOURCE: S.-W. Yang, Schering-Plough Research Institute, 2015 Galloping Hill Road, Kenilworth, NJ 07033, United States. shu-wei.yang@spcorp.com
SOURCE: Journal of Antibiotics, (1 Apr 2003) 56/4 (419-422). Refs: 7
ISSN: 0021-8820 CODEN: JANTAJ
COUNTRY: Japan
DOCUMENT TYPE: Journal; Note
FILE SEGMENT: 004 Microbiology
037 Drug Literature Index
LANGUAGE: English

L12 ANSWER 3 OF 38 EMBASE COPYRIGHT 2003 ELSEVIER SCI. B.V.
ACCESSION NUMBER: 2002214779 EMBASE
TITLE: The clinical spectrum of pulmonary aspergillosis.
AUTHOR: Soubani A.O.; Chandrasekar P.H.
CORPORATE SOURCE: Dr. A.O. Soubani, Harper University Hospital, Division of Pulmonary Medicine, 3990 John R-3 Hudson,

Detroit, MI 48201, United States.
asoubani@intmed.wayne.edu
SOURCE: Chest, (2002) 121/6 (1988-1999).
Refs: 145
ISSN: 0012-3692 CODEN: CHETBF
COUNTRY: United States
DOCUMENT TYPE: Journal; General Review
FILE SEGMENT: 015 Chest Diseases, Thoracic Surgery and Tuberculosis
026 Immunology, Serology and Transplantation
030 Pharmacology
037 Drug Literature Index
038 Adverse Reactions Titles
LANGUAGE: English
SUMMARY LANGUAGE: English
AB Aspergillus is a ubiquitous fungus that causes a variety of clinical syndromes in the lung, ranging from aspergilloma in patients with lung cavities, to chronic necrotizing aspergillosis in those who are mildly immunocompromised or have chronic lung disease. Invasive pulmonary aspergillosis (IPA) is a severe and commonly fatal disease that is seen in immunocompromised patients, while allergic bronchopulmonary aspergillosis is a hypersensitivity reaction to Aspergillus antigens that mainly affects patients with asthma. In light of the increasing risk factors leading to IPA, such as organ transplantation and immunosuppressive therapy, and recent advances in the diagnosis and treatment of Aspergillus-related lung diseases, it is essential for clinicians to be familiar with the clinical presentation, diagnostic methods, and approach to management of the spectrum of pulmonary aspergillosis.

L12 ANSWER 4 OF 38 EMBASE COPYRIGHT 2003 ELSEVIER SCI. B.V.
ACCESSION NUMBER: 2002385973 EMBASE
TITLE: Successful treatment with caspofungin of hepatosplenic candidiasis resistant to liposomal amphotericin B [2].
AUTHOR: Sora F.; Chiusolo P.; Piccirillo N.; Pagano L.; Laurenti L.; Farina G.; Sica S.; Leone G.
CORPORATE SOURCE: Dr. S. Sica, Divisione di Ematologia, Istituto di Semeiotica Medica, Universita Cattolica Sacro Cuore, Largo A. Gemelli 8, 00168 Rome, Italy.
emacat@rm.unicatt.it
SOURCE: Clinical Infectious Diseases, (1 Nov 2002) 35/9 (1135-1136).
Refs: 6
ISSN: 1058-4838 CODEN: CIDIEL
COUNTRY: United States
DOCUMENT TYPE: Journal; Letter
FILE SEGMENT: 004 Microbiology
037 Drug Literature Index
048 Gastroenterology
LANGUAGE: English

L12 ANSWER 5 OF 38 EMBASE COPYRIGHT 2003 ELSEVIER SCI. B.V.
ACCESSION NUMBER: 2003035131 EMBASE
TITLE: Aspergillus infections in allogeneic stem cell transplant recipients: Have we made any progres?.
AUTHOR: Jantunen E.; Anttila V.-J.; Ruutu T.
CORPORATE SOURCE: E. Jantunen, Department of Medicine, Kuopio

University Hospital, POB 1777, 70211 Kuopio, Finland
SOURCE: Bone Marrow Transplantation, (2002) 30/12 (925-929).
Refs: 65
ISSN: 0268-3369 CODEN: BMTRE
COUNTRY: United Kingdom
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 004 Microbiology
025 Hematology
030 Pharmacology
037 Drug Literature Index
038 Adverse Reactions Titles
LANGUAGE: English
SUMMARY LANGUAGE: English

AB Invasive aspergillosis (IA) is common in allogeneic SCT recipients, with an incidence of 4-10%. The majority of these infections are diagnosed several months after SCT and they are frequently associated with GVHD. The diagnosis is difficult and often delayed. Established IA is notoriously difficult to treat with a death rate of 80-90%. This review summarises recent data on this problem to assess whether there has been any progress. Effective prophylactic measures are still lacking. Severe immunosuppression is the main obstacle to the success of therapy. Recent and ongoing developments in diagnostic measures and new antifungal agents may improve treatment results to some extent, but Aspergillus infections still remain a formidable problem in allogeneic transplantation. Further studies in this field will focus on the role of various cytokines and combinations of antifungal agents.

L12 ANSWER 6 OF 38 MEDLINE DUPLICATE 1

ACCESSION NUMBER: 2002259572 MEDLINE
DOCUMENT NUMBER: 21993647 PubMed ID: 11999005
TITLE: Diagnosis and treatment of invasive pulmonary aspergillosis in neutropenic patients.
AUTHOR: Reichenberger F; Habicht J M; Gratwohl A; Tamm M
CORPORATE SOURCE: Division of Pneumology, Dept of Internal Medicine, University Hospital Leipzig, Germany.. reichenf@hotmail.com
SOURCE: EUROPEAN RESPIRATORY JOURNAL, (2002 Apr) 19 (4) 743-55. Ref: 142
Journal code: 8803460. ISSN: 0903-1936.
PUB. COUNTRY: Denmark
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
(REVIEW, TUTORIAL)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200210
ENTRY DATE: Entered STN: 20020510
Last Updated on STN: 20021024
Entered Medline: 20021023

AB Invasive pulmonary aspergillosis is a major cause of morbidity and mortality in neutropenic patients. Microbiological and serological tests are of limited value. The diagnosis should be considered in neutropenic patients with fever not responding to antibiotics, and typical findings on thoracic computed tomography scan. Whenever possible, diagnosis should be confirmed by tissue examination. Newer techniques, such as polymerase chain reaction may change the current diagnostic approach. Therapeutic strategies consist of

prophylaxis in risk groups and the early application of antifungal agents in suspected or probable disease. Amphotericin B as desoxycholate or lipid formulation is the current standard medication in invasive infection, although it has major side effects. Its role is challenged by the new azole derivates, such as itraconazole and voriconazole, and the new **echinocandins**. Additional therapies with cytokines, such as **granulocyte** macrophage colony stimulating factor and interferon-gamma, and with **granulocyte** transfusions are under evaluation. In selected cases lung resection is of proven diagnostic and therapeutic value. This paper analyses the current understanding of the pathogenesis and epidemiology of invasive aspergillosis and reviews the actual diagnostic and therapeutic strategies for invasive pulmonary aspergillosis in neutropenic patients.

L12 ANSWER 7 OF 38 EMBASE COPYRIGHT 2003 ELSEVIER SCI. B.V.
ACCESSION NUMBER: 2002290242 EMBASE
TITLE: Invasive fungal infections in the neutropenic cancer patient: Current approaches and future strategies.
AUTHOR: Groll A.H.; Walsh T.J.
SOURCE: Infections in Medicine, (2002) 19/7 (326-334).
Refs: 61
ISSN: 0749-6524 CODEN: INMDEG
COUNTRY: United States
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 004 Microbiology
016 Cancer
026 Immunology, Serology and Transplantation
030 Pharmacology
037 Drug Literature Index
038 Adverse Reactions Titles
LANGUAGE: English
SUMMARY LANGUAGE: English
AB Invasive fungal infections are important causes of morbidity and mortality in cancer patients with prolonged neutropenia following dose-intensive chemotherapy or hematopoietic stem cell transplantation. Recent epidemiologic trends indicate a shift toward infections by Aspergillus species, non-albicans Candida species, and previously uncommon fungal pathogens that have decreased susceptibility to current antifungal agents. In the last decade, much progress has been made in establishing disease definitions and paradigms for antifungal intervention and in the design and conduct of interventional clinical trials. This article reviews current approaches to prevention and treatment of opportunistic fungal infections in neutropenic patients and discusses novel approaches to antifungal chemotherapy and supportive measures.

L12 ANSWER 8 OF 38 EMBASE COPYRIGHT 2003 ELSEVIER SCI. B.V.
ACCESSION NUMBER: 2002116284 EMBASE
TITLE: Imaging findings in invasive zygomycosis.
AUTHOR: Singh N.
CORPORATE SOURCE: Dr. N. Singh, VA Medical Center Infect. Dis. Sec., Thomas E. Starzl Transplantion Inst., University Drive C, Pittsburgh, PA 15240, United States. nis5+@pitt.edu
SOURCE: Liver Transplantation, (2002) 8/3 (306-307).
Refs: 4
ISSN: 1527-6465 CODEN: LITRFO

COUNTRY: United States
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 004 Microbiology
009 Surgery
026 Immunology, Serology and Transplantation
037 Drug Literature Index
048 Gastroenterology
LANGUAGE: English

L12 ANSWER 9 OF 38 EMBASE COPYRIGHT 2003 ELSEVIER SCI. B.V.
ACCESSION NUMBER: 2002332283 EMBASE
TITLE: Antifungal chemotherapy: Advances and perspectives.
AUTHOR: Groll A.H.; Walsh T.J.
CORPORATE SOURCE: Dr. A.H. Groll, Ctr. for Bone Marrow Transplantation, Dept. of Pediatric Haematology, University Medical Center, Domagkstrasse 9a, D-48129 Muenster, Germany. grollan@mednet.uni-muenster.de
SOURCE: Swiss Medical Weekly, (15 Jun 2002) 132/23-24 (303-311).
Refs: 103
ISSN: 1424-7860 CODEN: SMWWAI
COUNTRY: Switzerland
DOCUMENT TYPE: Journal; (Short Survey)
FILE SEGMENT: 004 Microbiology
037 Drug Literature Index
038 Adverse Reactions Titles
039 Pharmacy
LANGUAGE: English
SUMMARY LANGUAGE: English

AB Invasive fungal infections have emerged as important causes of morbidity and mortality in immunocompromised patients. In response to this challenge, the field of antifungal chemotherapy has considerably expanded. Fluconazole and itraconazole, introduced in the late 1980s, were the first durably useful alternatives to amphotericin B deoxycholate. The clinical development of the lipid formulations of amphotericin B, and, more recently, that of novel **echinocandin** derivatives and improved antifungal triazoles each represent milestones in antifungal drug research that have further amplified our therapeutic options. Major progress has been made in harmonising disease definitions, in defining the paradigms of antifungal intervention, and in designing and implementing clinical trials. Standardised methods for in vitro susceptibility testing of yeasts and filamentous fungi have become available, and pharmacodynamic concepts have entered preclinical and clinical drug development. This article reviews the evolution of therapeutic options over the past decade, advances in chemoprevention and empirical antifungal therapy, progress in early diagnosis and pre-emptive therapy, the promise of the new **echinocandins** and second generation triazoles, as well as perspectives for combination therapies and adjuvant immunoreconstitution. Invasive fungal infections will remain a frequent and important complication of modern medicine; the current momentum in the field of laboratory and clinical antifungal drug research provides hope for substantial progress in prevention and management of these life-threatening infections in the near future.

L12 ANSWER 10 OF 38 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC.
ACCESSION NUMBER: 2002:552494 BIOSIS

DOCUMENT NUMBER: PREV200200552494
TITLE: New drugs, old drugs - dear drugs, cheap drugs.
AUTHOR(S): Hirschel, Bernard (1); Garbino, Jorge
CORPORATE SOURCE: (1) Division des Maladies Infectieuses, Hopital Cantonal Universitaire, CH-1211, Geneve 14: bernard.hirschel@hcuge.ch Switzerland
SOURCE: Swiss Medical Weekly, (June 15, 2002) Vol. 132, No. 23-24, pp. 301-302. print.
ISSN: 1424-7860.
DOCUMENT TYPE: Article
LANGUAGE: English

L12 ANSWER 11 OF 38 EMBASE COPYRIGHT 2003 ELSEVIER SCI. B.V.
ACCESSION NUMBER: 2002144324 EMBASE
TITLE: Invasive aspergillosis in 2002: An update.
AUTHOR: Kontoyiannis D.P.; Bodey G.P.
CORPORATE SOURCE: D.P. Kontoyiannis, Department of Infectious Diseases, Box 402, Univ. Texas M.D. Anderson Can. Ctr., 1515 Holcombe Boulevard, Houston, TX 77030, United States. dkontoyi@mdanderson.org
SOURCE: European Journal of Clinical Microbiology and Infectious Diseases, (2002) 21/3 (161-172).
Refs: 109
ISSN: 0934-9723 CODEN: EJCDEU
COUNTRY: Germany
DOCUMENT TYPE: Journal; General Review
FILE SEGMENT: 004 Microbiology
030 Pharmacology
037 Drug Literature Index
LANGUAGE: English
SUMMARY LANGUAGE: English
AB Despite significant advances in the management of immunosuppressed patients, invasive aspergillosis remains an important life-threatening complication. In the past two decades, the incidence of invasive aspergillosis in this population has continued to increase. Factors that predispose patients to develop invasive aspergillosis include prolonged **granulocytopenia**, the development of graft-versus-host disease, immunosuppressive therapy, the use of adrenal corticosteroids, and the prolonged impairment of host defenses associated with diseases such as chronic **granulomatous** disease. Environmental factors also play a key part in the pathogenesis of this infection, and therefore, infection control measures play a critical role in reducing exposure of patients to Aspergillus. New exciting developments in the early diagnosis of invasive aspergillosis and the acceleration of antifungal drug discovery offer promise for the future.

L12 ANSWER 12 OF 38 WPIDS (C) 2003 THOMSON DERWENT
ACCESSION NUMBER: 2001-607108 [69] WPIDS
DOC. NO. CPI: C2001-180350
TITLE: Nasally administered composition for treating and prophylaxis of mycoses and disease comprises a cyclic peptide adsorbed onto a **powdery** or crystalline polyvalence metal or organic carrier.
DERWENT CLASS: A11 A14 A96 B02 B04 C02 C03 P34
INVENTOR(S): HORII, I; IANAGAWA, A; KOBAYASHI, K; SHIMMA, N; YANAGAWA, A
PATENT ASSIGNEE(S): (BASI-N) BASILEA PHARM AG; (HORI-I) HORII I;

(KOBA-I) KOBAYASHI K; (SHIM-I) SHIMMA N; (YANA-I) YANAGAWA A

COUNTRY COUNT: 90

PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
WO 2001052894	A2	20010726	(200169)*	EN	117
RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW MZ NL OA PT SD SE SL SZ TR TZ UG ZW					
W: AE AL AM AT AU AZ BA BB BG BR BY CA CH CN CU CZ DE DK EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT UA UG UZ VN YU ZA ZW					
AU 2001037280	A	20010731	(200171)		
US 2001038824	A1	20011108	(200171)		
EP 1251827	A2	20021030	(200279)	EN	
R: AL AT BE CH CY DE DK ES FI FR GB GR IE IT LI LT LU LV MC MK NL PT RO SE SI TR					
BR 2001007764	A	20021112	(200281)		
KR 2002070346	A	20020905	(200311)		

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
WO 2001052894	A2	WO 2001-EP163	20010109
AU 2001037280	A	AU 2001-37280	20010109
US 2001038824	A1	US 2001-765846	20010119
EP 1251827	A2	EP 2001-909587	20010109
		WO 2001-EP163	20010109
BR 2001007764	A	BR 2001-7764	20010109
		WO 2001-EP163	20010109
KR 2002070346	A	KR 2002-709360	20020720

FILING DETAILS:

PATENT NO	KIND		PATENT NO
AU 2001037280	A	Based on	WO 200152894
EP 1251827	A2	Based on	WO 200152894
BR 2001007764	A	Based on	WO 200152894

PRIORITY APPLN. INFO: EP 2000-101057 20000120

AN 2001-607108 [69] WPIDS

AB WO 200152894 A UPAB: 20011126

NOVELTY - Nasally administrable composition (A) comprises a physiologically active cyclic peptide and a **powdery** or crystalline carrier comprising a polyvalence metal or an organic carrier. The cyclic peptide is dispersed homogeneously in and adsorbed onto the carrier, which has a mean particle size of 20-500 micro m.

DETAILED DESCRIPTION - An INDEPENDENT CLAIM is also included for preparation of (A) by homogeneously dispersing the cyclic peptide in the carrier optionally in the presence of an absorption enhancer, and adsorbing the peptide onto the carrier.

ACTIVITY - Antibacterial; fungicide.

MECHANISM OF ACTION - None given

USE - To treat disease and for treatment or prophylaxis of mycoses (claimed).
Dwg.0/11

L12 ANSWER 13 OF 38 EMBASE COPYRIGHT 2003 ELSEVIER SCI. B.V.
ACCESSION NUMBER: 2001326803 EMBASE
TITLE: Therapeutic options for acute myelogenous leukemia.
AUTHOR: Estey E.H.
CORPORATE SOURCE: Dr. E.H. Estey, Department of Leukemia, University of Texas, M.D. Anderson Cancer Center, 1400 Holcombe Blvd., Houston, TX 77030-4095, United States. ehestey@mdanderson.org
SOURCE: Cancer, (1 Sep 2001) 92/5 (1059-1073).
Refs: 78
ISSN: 0008-543X CODEN: CANCAR
COUNTRY: United States
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 016 Cancer
025 Hematology
037 Drug Literature Index
LANGUAGE: English
SUMMARY LANGUAGE: English
AB BACKGROUND. General therapeutic options for patients with acute myelogenous leukemia (AML) are reviewed and specific new therapies are described. METHODS. Data in this review came from the published literature and the M. D. Anderson Cancer Center's acute leukemia database. RESULTS. Outcome following standard therapy of AML is so variable that is best to speak of a range of outcomes determined by various prognostic factors. Therapy can (and usually does) fail because of treatment-induced mortality or (more usually) resistance to therapy. Performance status and age are the principal predictors of early death, whereas cytogenetics, a history of abnormal blood counts, and MDR1 expression are predictors of resistance. Using this information, physicians can categorize patients into those in whom 1) standard therapy is indicated, 2) either standard or investigational therapy is appropriate, and 3) investigational therapy is indicated. The majority of even newly diagnosed patients belong to Group 3. The availability of allogeneic or autologous transplantation does not alter this conclusion. Investigational therapies have been developed that are directed against the CD33 surface antigen, the multidrug-resistant MDR1 protein, and other targets. Because of the number of new therapies clinical research in AML should emphasize pilot trials rather than traditionally large Phase III studies. CONCLUSIONS. Most patients with newly diagnosed AML should be offered investigational regimens. .COPYRGT. 2001 American Cancer Society.

L12 ANSWER 14 OF 38 EMBASE COPYRIGHT 2003 ELSEVIER SCI. B.V.
ACCESSION NUMBER: 2001173809 EMBASE
TITLE: [Antifungal drugs in the treatment of systemic candidiosis: Susceptibility to antifungal drugs, point on drug resistance, pharmacological data]. UTILISATION DES ANTIFONGIQUES DANS LE TRAITEMENT DES CANDIDOSES SYSTEMIQUES: ANTIFONGIGRAMME, POINT SUR LES RESISTANCES, DONNEES PHARMACOLOGIQUES.
AUTHOR: Datry A.; Thellier M.; Traore B.; Alfa Cisse O.; Danis M.
CORPORATE SOURCE: A. Datry, Service de Parasitologie-Mycologie, CHU

Pitie-Salpetriere, 47-83, bd de l'Hopital, 75013 Paris, France
SOURCE: Annales Francaises d'Anesthesie et de Reanimation, (2001) 20/4 (389-393).
Refs: 17
ISSN: 0750-7658 CODEN: AFAREO
COUNTRY: France
DOCUMENT TYPE: Journal; General Review
FILE SEGMENT: 004 Microbiology
037 Drug Literature Index
039 Pharmacy
LANGUAGE: French
SUMMARY LANGUAGE: English; French
AB The available antifungal agents are amphotericin B (conventional or lipid formulation), flucytosin and azole derivatives (ketoconazole, fluconazole, itraconazole). The main target of these molecules are a specific compound of fungal membrane, ergosterol. Determination of the fungal sensitivity to antifungal drugs is difficult and no consensus has been achieved so far. Minimal inhibitory concentrations are poor predictors of clinical success or failure. A good correlation between in vitro and in vivo results has been observed only in patients with oropharyngeal candidiasis associated with HIV infection. Combinations of antifungal drugs are currently under study. The role of hemopoietic growth factors (G-CSF, GM-CSF) as an adjuvant has not been fully established. New antifungal drugs (triazole derivatives, **echinocandins**) should be available within months. .COPYRGT. 2001 Editions scientifiques et medicales Elsevier SAS.

L12 ANSWER 15 OF 38 EMBASE COPYRIGHT 2003 ELSEVIER SCI. B.V.
ACCESSION NUMBER: 2002024113 EMBASE
TITLE: Fungal infections in the organ transplant recipient.
AUTHOR: Avery R.K.
CORPORATE SOURCE: Dr. R.K. Avery, Department of Infectious Diseases, Desk S32, Cleveland Clinic Foundation, 9500 Euclid Avenue, Cleveland, OH 44195, United States. averyr@ccf.org
SOURCE: Current Opinion in Organ Transplantation, (2001) 6/4 (284-289).
Refs: 84
ISSN: 1087-2418 CODEN: COOTAB
COUNTRY: United States
DOCUMENT TYPE: Journal; General Review
FILE SEGMENT: 026 Immunology, Serology and Transplantation
004 Microbiology
009 Surgery
017 Public Health, Social Medicine and Epidemiology
030 Pharmacology
038 Adverse Reactions Titles
039 Pharmacy
037 Drug Literature Index
LANGUAGE: English
SUMMARY LANGUAGE: English
AB Fungal infections constitute some of the most difficult clinical management problems encountered after solid organ transplantation. Although the predominant pathogens continue to be Candida species followed by Aspergillus species, emerging fungal pathogens including

azole-resistant yeast, Fusarium, and dematiaceous fungi are becoming more significant. Identification of novel risk factors has expanded traditional concepts of the epidemiology of these infections. Optimal prophylaxis of fungal infections constitutes an area of active research. Diagnosis continues to be a challenge, but newer methods including antigen assays and panfungal or specific fungal polymerase chain reaction methodology are promising. Advances in therapy include lipid amphotericin formulations, newer azoles such as voriconazole, ravuconazole, and posaconazole, and **echinocandins** such as the recently approved drug caspofungin, as well as immunomodulatory therapy. .COPYRGT. 2001 Lippincott Williams & Wilkins, Inc.

L12 ANSWER 16 OF 38 EMBASE COPYRIGHT 2003 ELSEVIER SCI. B.V.
ACCESSION NUMBER: 2001317385 EMBASE
TITLE: Infections after stem cell transplantation in children: State of the art and recommendations.
AUTHOR: Dini G.; Castagnola E.; Comoli P.; Van Tol M.J.D.; Vossen J.M.
CORPORATE SOURCE: G. Dini, Department of Hemato-Oncology, Bone Marrow Transplantation Children, Istituto Giannina Gaslini, Genoa, Italy
SOURCE: Bone Marrow Transplantation, (2001) 28/SUPPL. 1 (S18-S21).
Refs: 19
ISSN: 0268-3369 CODEN: BMTRE
COUNTRY: United Kingdom
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 004 Microbiology
007 Pediatrics and Pediatric Surgery
025 Hematology
037 Drug Literature Index
LANGUAGE: English
SUMMARY LANGUAGE: English
AB At the workshop on infections after stem cell transplantation (SCT) in children, the following topics were introduced by invited speakers and discussed with the audience: empirical antimicrobial therapy in the pre-engraftment period, early diagnosis of fungal and viral infections and possibilities to treat them and the possible role of G-CSF early post-SCT. Episodes of fever in the pre-engraftment period mostly are unexplained, and in about one quarter due to bacteremia, mostly by Gram-positive cocci. No single drug or combination of drugs used for antimicrobial therapy is superior, neither does it cover 100% of the pathogens. Close microbiological surveillance of the patients and knowledge of the local microbial epidemiology are requested for optimal therapy. Early fungal infections are reactivations of pre-SCT infections, late fungal infections mostly are associated with failure of engraftment or GvHD and its treatment. Except for suggestive ultrasound or CT-scan abnormalities, the possibilities for early diagnosis are limited c.q. not reliable. Fluconazol prophylaxis is recommended to prevent Candida albicans invasion. A number of new antifungal drugs are being tested in phase I and II studies. CMV, EBV and adenoviruses may reactivate after SCT, causing severe disease with a high mortality, especially in non-HLA-identical donor-recipient combinations. Frequent surveillance cultures for CMV and adenoviruses, pp65-CMV antigen detection in WBC and PCR techniques for CMV, EBV and adenoviruses all have their own

contribution to the early diagnosis of dissemination of the viral infection. Therapeutical possibilities, except with respect to ganciclovir and foscarnet for CMV infection, are still limited. The effectiveness of cidofovir is under study. Adoptive therapy with virus-specific CTL's probably represents the new frontier. G-CSF administration early after SCT has a beneficial effect on PMN recovery, hospitalization time, use of antibiotics and total parenteral nutrition requirement in children undergoing allogeneic and autologous BMT. No benefit is observed in children undergoing peripheral blood SCT. The routine use of G-CSF in the latter group of patients is not justified.

L12 ANSWER 17 OF 38 EMBASE COPYRIGHT 2003 ELSEVIER SCI. B.V.

ACCESSION NUMBER: 2002310484 EMBASE
TITLE: Uncommon opportunistic fungi: New nosocomial threats.
AUTHOR: Groll A.H.; Walsh T.J.
CORPORATE SOURCE: Dr. A.H. Groll, Immunocompromised Host Section, National Cancer Institute, Bldg. 10, Bethesda, MD 20892, United States. grolla@mail.nih.gov
SOURCE: Clinical Microbiology and Infection, (2001) 7/SUPPL. 2 (8-24).
Refs: 206
ISSN: 1198-743X CODEN: CMINFM
COUNTRY: United Kingdom
DOCUMENT TYPE: Journal; General Review
FILE SEGMENT: 004 Microbiology
026 Immunology, Serology and Transplantation
030 Pharmacology
037 Drug Literature Index
038 Adverse Reactions Titles
LANGUAGE: English
SUMMARY LANGUAGE: English

AB During the past two decades opportunistic fungal infections have emerged as important causes of morbidity and mortality in patients with severe underlying illnesses and compromised host defenses. While Aspergillus and Candida spp. collectively account for the majority of these infections, recent epidemiological trends indicate a shift towards infections by Aspergillus spp., nonalbicans Candida spp., as well as previously uncommon opportunistic fungi. Apart from an expanding number of different Zygomycetes, previously uncommon hyaline filamentous fungi (such as Fusarium species, Acremonium species, Paecilomyces species, Pseudallescheria boydii, and Scedosporium prolificans), dematiaceous filamentous fungi (such as Bipolaris species, Cladophialophora bantiana, Dactylaria gallopava, Exophiala species, and Alternaria species) and yeast-like pathogens (such as Trichosporon species, Blastoschizomyces capitatus, Malassezia species, Rhodotorula rubra and others) are increasingly encountered as causing life threatening invasive infections that are often refractory to conventional therapies. On the basis of past and current trends, the spectrum of fungal pathogens will continue to evolve in the settings of an expanding population of immunocompromised hosts, selective antifungal pressures, and shifting conditions in hospitals and the environment. An expanded and refined drug arsenal, further elucidation of pathogenesis and resistance mechanisms, establishment of in vitro/in vivo correlations, incorporation of pharmacodynamics, combination- and immunotherapies offer hope for substantial progress in prevention and treatment.

L12 ANSWER 18 OF 38 WPIDS (C) 2003 THOMSON DERWENT
ACCESSION NUMBER: 2000-594167 [56] WPIDS
DOC. NO. CPI: C2000-177397
TITLE: New thermally stable, water-soluble carbohydrate complexes of **echinocandins**, useful as antiprotozoal and especially antifungal agents suitable for parenteral administration.
DERWENT CLASS: B02 C02
INVENTOR(S): LAREW, L A; MILTON, N; MODER, K P; SABATOWSKI, J L
PATENT ASSIGNEE(S): (ELIL) LILLY & CO ELI; (LARE-I) LAREW L A; (MILT-I) MILTON N; (MODE-I) MODER K P; (SABA-I) SABATOWSKI J L
COUNTRY COUNT: 90
PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
WO 2000052037	A1	20000908	(200056)*	EN	35
RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW NL OA PT SD SE SL SZ TZ UG ZW					
W: AE AL AM AT AU AZ BA BB BG BR BY CA CH CN CR CU CZ DE DK EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT TZ UA UG US UZ VN YU ZA ZW					
AU 2000038635	A	20000921	(200065)		
EP 1157030	A1	20011128	(200201)	EN	
R: AL AT BE CH CY DE DK ES FI FR GB GR IE IT LI LT LU LV MC MK NL PT RO SE SI					
BR 2000008712	A	20011226	(200206)		
KR 2002003864	A	20020115	(200247)		
CN 1345333	A	20020417	(200248)		
US 2002160942	A1	20021031	(200274)		
JP 2002539090	W	20021119	(200281)		50

APPLICATION DETAILS:

PATENT NO	KIND		APPLICATION	DATE
WO 2000052037	A1		WO 2000-US5508	20000302
AU 2000038635	A		AU 2000-38635	20000302
EP 1157030	A1		EP 2000-917703	20000302
			WO 2000-US5508	20000302
BR 2000008712	A		BR 2000-8712	20000302
			WO 2000-US5508	20000302
KR 2002003864	A		KR 2001-711234	20010903
CN 1345333	A		CN 2000-805697	20000302
US 2002160942	A1	Provisional	US 1999-122692P	19990303
		Cont of	WO 2000-US5508	20000302
			US 2001-942458	20010829
JP 2002539090	W		JP 2000-602261	20000302
			WO 2000-US5508	20000302

FILING DETAILS:

PATENT NO	KIND		PATENT NO
AU 2000038635	A	Based on	WO 200052037

Searcher : Shears 308-4994

EP 1157030 A1 Based on WO 200052037
BR 2000008712 A Based on WO 200052037
JP 2002539090 W Based on WO 200052037

PRIORITY APPLN. INFO: US 1999-122692P 19990303; US 2001-942458 20010829
AN 2000-594167 [56] WPIDS
AB WO 200052037 A UPAB: 20010410
NOVELTY - **Echinocandin**-carbohydrate complexes (A) are new.
DETAILED DESCRIPTION - New complexes (A) comprise a carbohydrate (I) and an **echinocandin** (EC) compound of formula (II) or its salt or hydrate.
R = alkyl, alkenyl, alkynyl, aryl, heteroaryl or a combination of these groups;
R1-R3, R6, R7, R10 = H or OH;
R4 = H, Me or CH2CONH2;
R5, R11 = Me or H;
R8 = OH, OSO3H, OPO3H2, OPO3HRa or OPO2HRa;
Ra = OH, 1-6C alkyl, 1-6C alkoxy, Ar, OAr, CH2Ar or OCH2Ar;
Ar = phenyl, p-halophenyl or p-nitrophenyl;
R9 = H, OH or OSO3H.
An INDEPENDENT CLAIM is included for (A) in terms of its preparation.
ACTIVITY - Antifungal; protozoacide.
MECHANISM OF ACTION - None given.
USE - (A) are used for treating fungal infections, specifically Candida albicans or Aspergillus fumigatus infections (all claimed). They are useful for combating systemic or skin fungal infections. (A) are also effective against organisms causing opportunistic infections in immunosuppressed (e.g. acquired immunodeficiency syndrome (AIDS)) patients, such as Pneumonocystis carinii (causing pneumocystis pneumonia); and protozoans such as Plasmodium, Leishmania, Trypanosoma, Cryptosporidium, Isospora, Cyclospora, Trichomonas or Microsporidiosis.
No activity example is given.
ADVANTAGE - (A) are crystalline complexes which collapse to an amorphous form when contacted with body fluids, are readily purified and have improved thermal stability and water solubility compared with the parent EC active compounds (II). The improved water solubility is obtained without reduction of bioavailability or the need for structural modification; and makes (A) especially suitable for use in parenteral (e.g. intraperitoneal) formulations. In a thermal stability test a complex of EC B with 4 equivalents of D-**fructose** retained 83.4% of its potency after storage in a sealed vial at 50 deg. C for 2 weeks.
Dwg.0/0

L12 ANSWER 19 OF 38 WPIDS (C) 2003 THOMSON DERWENT
ACCESSION NUMBER: 2001-015543 [02] WPIDS
DOC. NO. CPI: C2001-004080
TITLE: Stable **granular** oral antifungal and antiparasitic formulations, obtained by spraying solution containing **echinocandin** and carbohydrate onto fluidized carrier.
DERWENT CLASS: A96 B02 C01 C02
INVENTOR(S): SCHWIER, J R; TAYLOR, J
PATENT ASSIGNEE(S): (ELIL) LILLY & CO ELI; (SCHW-I) SCHWIER J R; (TAYL-I) TAYLOR J

Searcher : Shears 308-4994

COUNTRY COUNT: 91
PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
WO 2000051567	A1	20000908	(200102)*	EN	40
RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW NL OA PT SD SE SL SZ TZ UG ZW					
W: AE AL AM AT AU AZ BA BB BG BR BY CA CH CN CR CU CZ DE DK DM EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT TZ UA UG US UZ VN YU ZA ZW					
AU 2000033934	A	20000921	(200102)		
EP 1156784	A1	20011128	(200201)	EN	
R: AL AT BE CH CY DE DK ES FI FR GB GR IE IT LI LT LU LV MC MK NL PT RO SE SI					
BR 2000008713	A	20011226	(200206)		
KR 2001112302	A	20011220	(200239)		
CN 1345230	A	20020417	(200248)		
US 2002151474	A1	20021017	(200270)		
JP 2002538097	W	20021112	(200275)		48

APPLICATION DETAILS:

PATENT NO	KIND		APPLICATION	DATE
WO 2000051567	A1		WO 2000-US5547	20000302
AU 2000033934	A		AU 2000-33934	20000302
EP 1156784	A1		EP 2000-912160	20000302
			WO 2000-US5547	20000302
BR 2000008713	A		BR 2000-8713	20000302
			WO 2000-US5547	20000302
KR 2001112302	A		KR 2001-711216	20010903
CN 1345230	A		CN 2000-805698	20000302
US 2002151474	A1	Provisional	US 1999-122693P	19990303
		Cont of	WO 2000-US5547	20000302
			US 2001-942435	20010829
JP 2002538097	W		JP 2000-602036	20000302
			WO 2000-US5547	20000302

FILING DETAILS:

PATENT NO	KIND		PATENT NO
AU 2000033934	A	Based on	WO 200051567
EP 1156784	A1	Based on	WO 200051567
BR 2000008713	A	Based on	WO 200051567
JP 2002538097	W	Based on	WO 200051567

PRIORITY APPLN. INFO: US 1999-122693P 19990303; US 2001-942435 20010829

AN 2001-015543 [02] WPIDS

AB WO 200051567 A UPAB: 20020613
NOVELTY - Preparation of an oral pharmaceutical formulation (A) comprises: (a) mixing an **echinocandin** compound (I) (optionally as a carbohydrate complex), carbohydrate(s) (II) in a solvent (or solvent mixture), (b) spraying the obtained solution weight onto a fluidized layer of **granular** diluent or

carrier (III) and (c) removing excess solvent(s) to form **granules.**

DETAILED DESCRIPTION - INDEPENDENT CLAIMS are included for:

(i) a variant on the process, in which the mixture in (a) further contains a soluble **granulating** agent (IV) and (III) is replaced by a non-**granular** diluent or carrier (III');

(ii) (A) obtained by the processes; and

(iii) medicaments comprising (A).

USE - For treating fungal infections (claimed), especially systemic or skin infections by Candida albicans or Aspergillus fumigatus infections. (I) are also effective against organisms causing opportunistic infections in immunosuppressed (e.g. AIDS) patients, such as Pneumonocystis carinii (causing pneumocystis pneumonia); and protozoans such as Plasmodium, Leishmania, Trypanosoma, Cryptosporidium, Isospora, Cyclospora, Trichomonas or Microsporidiosis.

ADVANTAGE - Inclusion of (II) markedly enhances the thermal stability of (I).

Dwg.0/0

L12 ANSWER 20 OF 38 WPIDS (C) 2003 THOMSON DERWENT
ACCESSION NUMBER: 2000-579205 [54] WPIDS
DOC. NO. CPI: C2000-172393
TITLE: Aqueous parenteral antifungal and antiparasitic formulations containing **echinocandin,** also containing micelle-forming surfactant to enhance drug solubility and stability.
DERWENT CLASS: A96 B02 C01 C02
INVENTOR(S): MILTON, N; MODER, K P; SABATOWSKI, J L; SWEETANA, S A
PATENT ASSIGNEE(S): (ELIL) LILLY & CO ELI; (MILT-I) MILTON N; (MODE-I) MODER K P; (SABA-I) SABATOWSKI J L; (SWEE-I) SWEETANA S A
COUNTRY COUNT: 91
PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
WO 2000051564	A1	20000908	(200054)*	EN	44
RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW NL OA PT SD SE SL SZ TZ UG ZW					
W: AE AL AM AT AU AZ BA BB BG BR BY CA CH CN CR CU CZ DE DK DM EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT TZ UA UG US UZ VN YU ZA ZW					
AU 2000032491	A	20000921	(200065)		
EP 1156782	A1	20011128	(200201)	EN	
R: AL AT BE CH CY DE DK ES FI FR GB GR IE IT LI LT LU LV MC MK NL PT RO SE SI					
BR 2000009249	A	20011120	(200202)		
KR 2001111570	A	20011219	(200238)		
CN 1345229	A	20020417	(200248)		
JP 2002538095	W	20021112	(200275)		53
US 2003054981	A1	20030320	(200323)		

APPLICATION DETAILS:

PATENT NO	KIND		APPLICATION	DATE
WO 2000051564	A1		WO 2000-US5546	20000302
AU 2000032491	A		AU 2000-32491	20000302
EP 1156782	A1		EP 2000-910391	20000302
			WO 2000-US5546	20000302
BR 2000009249	A		BR 2000-9249	20000302
			WO 2000-US5546	20000302
KR 2001111570	A		KR 2001-711215	20010903
CN 1345229	A		CN 2000-805696	20000302
JP 2002538095	W		JP 2000-602034	20000302
			WO 2000-US5546	20000302
US 2003054981	A1	Provisional	US 1999-122623P	19990303
		Cont of	WO 2000-US5546	20000302
			US 2001-942431	20010829

FILING DETAILS:

PATENT NO	KIND		PATENT NO
AU 2000032491	A	Based on	WO 200051564
EP 1156782	A1	Based on	WO 200051564
BR 2000009249	A	Based on	WO 200051564
JP 2002538095	W	Based on	WO 200051564

PRIORITY APPLN. INFO: US 1999-122623P 19990303; US 2001-942431 20010829

AN 2000-579205 [54] WPIDS

AB WO 200051564 A UPAB: 20020613

NOVELTY - A novel parenteral pharmaceutical formulation (A) comprises an **echinocandin** compound (I) (or its salt), a micelle-forming surfactant (II) and an aqueous solvent (III). The weight ratio of (I) to (II) is 1 : 1.75-25 and the (I) concentration is at least 1 mg/ml.

DETAILED DESCRIPTION - INDEPENDENT CLAIMS are included for:

(i) a freeze-dried formulation (B) comprising (I) (or its salt), (II) (in an amount of more than 5 wt. %) and a bulking agent (IV);

(ii) the preparation of (A) by mixing appropriate amounts of (I) (optionally as a complex with a carbohydrate) and (II) in (III);

(iii) the preparation of (B) (with no restriction on the (II) content) by buffering (III), adding (II), cooling to 5-15 deg. C, adding a slurry of (I) (optionally as a complex with a carbohydrate) in (III), sterile filtering and freeze-drying;

(iv) a parenteral formulation comprising (B) and (III); and

(v) a parenteral product obtained by dissolving (I) (optionally as a complex with a carbohydrate) in (III) in present of more than 1 % w/v of (II), sterile-filtering and freeze-drying in a vial.

USE - For treating fungal infections (claimed), especially systemic or skin infections by Candida albicans or Aspergillus fumigatus infections. (I) are also effective against organisms causing opportunistic infections in immunosuppressed (e.g. AIDS) patients, such as Pneumonocystis carinii (causing pneumocystis pneumonia); and protozoans such as Plasmodium, Leishmania, Trypanosoma, Cryptosporidium, Isospora, Cyclospora, Trichomonas or Microsporidiosis.

ADVANTAGE - (II) enhance the water-solubility and stability of (I), while retaining the ability to freeze-dry the formulation.

Addition of 25 mg/ml of polysorbate 80 increased the water-solubility of N-(4-(4'-(n-pentyloxy)-biphenyl-4-yl)-benzoyl) **echinocandin** B analog (Ia) from below 0.1 mg/ml to 13.2 mg/ml.
Dwg.0/0

L12 ANSWER 21 OF 38 MEDLINE DUPLICATE 2
ACCESSION NUMBER: 20010060788 MEDLINE
DOCUMENT NUMBER: 20548900 PubMed ID: 11099224
TITLE: FR901469, a novel antifungal antibiotic from an unidentified fungus No.11243. I. Taxonomy, fermentation, isolation, physico-chemical properties and biological properties.
AUTHOR: Fujie A; Iwamoto T; Muramatsu H; Okudaira T; Nitta K; Nakanishi T; Sakamoto K; Hori Y; Hino M; Hashimoto S; Okuhara M
CORPORATE SOURCE: Exploratory Research Laboratories, Fujisawa Pharmaceutical Co., Ltd., Tsukuba, Ibaraki, Japan.
SOURCE: JOURNAL OF ANTIBIOTICS, (2000 Sep) 53 (9) 912-9. Journal code: 0151115. ISSN: 0021-8820.
PUB. COUNTRY: Japan
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200012
ENTRY DATE: Entered STN: 20010322
Last Updated on STN: 20010322
Entered Medline: 20001222

AB FR901469 is a novel antifungal antibiotic produced by an unidentified fungus No.11243. This compound was isolated from the culture broth by solvent extraction, HP-20 and YMC ODS gel column chromatography, and lyophilization. FR901469 is a white **powder** which melts at 182 approximately 187 degrees C and possesses the molecular formula C71H116N14O23. This compound has good water solubility. FR901469 inhibited the activity of 1,3-beta-glucan synthase from Candida albicans with an IC50 value of 0.05 microg/ml, and displayed greater inhibitory activity than other 1,3-beta-glucan synthase inhibitors such as, WF11899A, **echinocandin** B, aculeacin A, and papulacandin B.

L12 ANSWER 22 OF 38 EMBASE COPYRIGHT 2003 ELSEVIER SCI. B.V.
ACCESSION NUMBER: 2001034525 EMBASE
TITLE: New advances in antifungal treatment.
AUTHOR: Finquelievich J.L.; Odds F.C.; Queiroz-Telles F.; Wheat L.J.
CORPORATE SOURCE: J.L. Finquelievich, Mycology Center, Univ. of Buenos Aires, British Hospital of Buenos Aires, Buenos Aires, Argentina. ctromic@janssen.com.ar
SOURCE: Medical Mycology, (2000) 38/SUPPL. 1 (317-322). Refs: 54
ISSN: 1369-3786 CODEN: MEMYFR
COUNTRY: United Kingdom
DOCUMENT TYPE: Journal; Conference Article
FILE SEGMENT: 004 Microbiology
038 Adverse Reactions Titles
030 Pharmacology
037 Drug Literature Index
026 Immunology, Serology and Transplantation

009 Surgery
015 Chest Diseases, Thoracic Surgery and Tuberculosis
036 Health Policy, Economics and Management
039 Pharmacy

LANGUAGE: English
SUMMARY LANGUAGE: English

AB Clinical aspects of treatment of invasive aspergillosis, infections caused by dematiaceous fungi, and mycoses caused by endemic, dimorphic fungi, are described in this review.

L12 ANSWER 23 OF 38 MEDLINE
ACCESSION NUMBER: 2000457229 MEDLINE
DOCUMENT NUMBER: 20464221 PubMed ID: 11012295
TITLE: Changing strategies for treatment of systemic mycoses.
AUTHOR: Graybill J R
CORPORATE SOURCE: Department of Medicine, Veterans Administration Hospital, San Antonio, TX 78284, USA.
SOURCE: BRAZILIAN JOURNAL OF INFECTIOUS DISEASES, (2000 Apr) 4 (2) 47-54. Ref: 67
Journal code: 9812937. ISSN: 1413-8670.
PUB. COUNTRY: Brazil
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
(REVIEW, TUTORIAL)
LANGUAGE: English
FILE SEGMENT: Priority Journals; AIDS
ENTRY MONTH: 200009
ENTRY DATE: Entered STN: 20001005
Last Updated on STN: 20001005
Entered Medline: 20000928

AB There have been a number of changes in strategies in antifungal therapy in the past few years. AIDS related mycoses have decreased, and the increase of fluconazole resistant Candida albicans may be slowing because fewer severely immune depressed patients require constant fluconazole suppression. Candida species continue to be relatively common blood culture isolates. About half of these are C. albicans and half non-albicans species. In recent years, we have moved from the use of amphotericin B to fluconazole for initial treatment of candidemia. We have seen fluconazole resistant isolates emerge, primarily C. glabrata and a few C. krusei, but also C. albicans. It is unclear whether the increasing use of fluconazole in intensive care units will worsen this problem. There appears to be no advantage for the lipid formulations of amphotericin B, though they are useful to reduce or prevent renal toxicity. In the United States and Europe, prevention and treatment of aspergillosis have become increasingly important. There are increasing data suggesting that lipid formulations are more effective for both treatment and prevention of invasive disease in the most vulnerable patients with this infection. Renal toxicity is reduced but not avoided by use of the lipid formulations of amphotericin B. For those patients with less acutely progressing disease, the triazoles may be effective options. It is unclear at present whether itraconazole, voriconazole, or posaconazole will be the most favored drug. One promising new class, now in clinical trials, is the **echinocandin** group. Other agents, such as the sordarins, the chitin synthase inhibitors, and topoisomerase

inhibitors, have promise but are much earlier in development. Unfortunately, we still have >50% treatment failure with acute invasive aspergillosis, and 20%-30% failures with candidemia. Now that we have multiple classes of antifungal drugs available, and others in preclinical trials, it would be advantageous to begin more active exploration of combination therapy with antifungals and with combined immune modulators and antifungals.

L12 ANSWER 24 OF 38 EMBASE COPYRIGHT 2003 ELSEVIER SCI. B.V.
ACCESSION NUMBER: 1999109940 EMBASE
TITLE: The changing face of nosocomial candidemia: Epidemiology, resistance, and drug therapy.
AUTHOR: Lewis R.E.; Klepser M.E.
CORPORATE SOURCE: Dr. M.E. Klepser, College of Pharmacy, S412 Pharmacy Building, University of Iowa, Iowa City, IA 52242-1112, United States. michael-klepser@ulowa.edu
SOURCE: American Journal of Health-System Pharmacy, (1 Mar 1999) 56/5 (525-536).
Refs: 90
ISSN: 1079-2082 CODEN: AHSPEK
COUNTRY: United States
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 004 Microbiology
037 Drug Literature Index
038 Adverse Reactions Titles
039 Pharmacy
LANGUAGE: English
SUMMARY LANGUAGE: English

AB The changing epidemiology and therapy of nosocomial candidemia are discussed. The frequency of nosocomial bloodstream infections by Candida species has risen dramatically in the past two decades. The arrival of antifungal drugs with better tolerability than conventional amphotericin B has resulted in widespread use of systemic antifungal therapy. With the introduction of new systemic antifungals, however, there have been major shifts in the epidemiology of candidal bloodstream infections toward species with less susceptibility to the available antifungal agents. Reports of in situ antifungal resistance are also becoming more common. Strategies for preventing the emergence of resistance have been suggested but have not undergone clinical trials. Antifungal susceptibility testing is becoming an increasingly important tool in the management of nosocomial candidemia. Treatments that have been undergoing investigation for use in these infections include combination therapies, lipid-based amphotericin B formulations, cytokines as adjuvant therapy, and novel antifungal agents such as voriconazole, SCH56592, and **echinocandins**. New antifungals in development may offer enhanced activity against pathogenic Candida species with less toxicity than amphotericin B. Antifungal susceptibility testing will play a major role in determining the treatment of resistant infections.

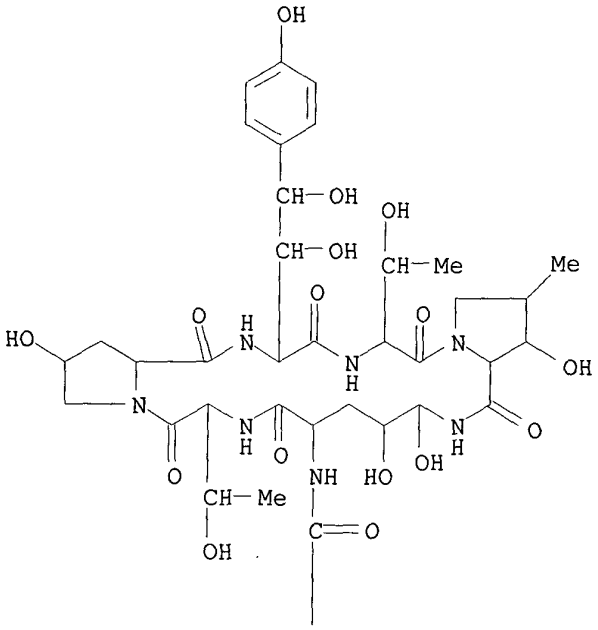
L12 ANSWER 25 OF 38 EMBASE COPYRIGHT 2003 ELSEVIER SCI. B.V.
ACCESSION NUMBER: 1999267506 EMBASE
TITLE: Fungal infections.
AUTHOR: Barnes R.A.
CORPORATE SOURCE: R.A. Barnes, Department of Medical Microbiology, University of Wales, College of Medicine, Cardiff CF4 4XN, United Kingdom

SOURCE: Current Anaesthesia and Critical Care, (1999) 10/1 (21-26).
Refs: 29
ISSN: 0953-7112 CODEN: CCCAEI
COUNTRY: United Kingdom
DOCUMENT TYPE: Journal; General Review
FILE SEGMENT: 004 Microbiology
017 Public Health, Social Medicine and Epidemiology
024 Anesthesiology
026 Immunology, Serology and Transplantation
029 Clinical Biochemistry
030 Pharmacology
037 Drug Literature Index
039 Pharmacy
038 Adverse Reactions Titles
LANGUAGE: English
SUMMARY LANGUAGE: English

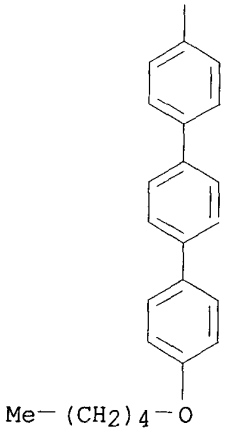
AB Systemic fungal infections are a rapidly increasing problem in critically ill patients and rates have increased significantly in the past 20 years. They represent a major cause of morbidity and mortality in a variety of hospitalized patients including those in neonatal and intensive care units. This trend concerns not only severely compromised hosts such as transplant recipients, neutropenic and HIV-positive patients, but also and non-compromised patients, on intensive care units (ICU) with specific risk factors for infection.

L12 ANSWER 26 OF 38 SCISEARCH COPYRIGHT 2003 THOMSON ISI
ACCESSION NUMBER: 1998:843929 SCISEARCH
THE GENUINE ARTICLE: 133NK
TITLE: Antifungal efficacy, safety, and single-dose pharmacokinetics of LY303366, a novel **echinocandin** B, in experimental pulmonary aspergillosis in persistently neutropenic rabbits
AUTHOR: Petraitis V; Petraitiene R; Groll A H; Bell A; Callender D P; Sein T; Schaufele R L; McMillian C L; Bacher J; Walsh T J (Reprint)
CORPORATE SOURCE: NCI, IMMUNOCOMPROMISED HOST SECT, PEDIAT ONCOL BRANCH, NIH, BLDG 10, RM 13N240, 10 CTR DR, BETHESDA, MD 20892 (Reprint); NCI, IMMUNOCOMPROMISED HOST SECT, PEDIAT ONCOL BRANCH, NIH, BETHESDA, MD 20892; NIH, NATL CTR RES RESOURCES, SURG BRANCH, VET RESOURCES SERV, BETHESDA, MD 20892; ELI LILLY & CO, LILLY RES LABS, INDIANAPOLIS, IN 46285
COUNTRY OF AUTHOR: USA
SOURCE: ANTIMICROBIAL AGENTS AND CHEMOTHERAPY, (NOV 1998) Vol. 42, No. 11, pp. 2898-2905.
Publisher: AMER SOC MICROBIOLOGY, 1325 MASSACHUSETTS AVENUE, NW, WASHINGTON, DC 20005-4171.
ISSN: 0066-4804.
DOCUMENT TYPE: Article; Journal
FILE SEGMENT: LIFE
LANGUAGE: English
REFERENCE COUNT: 30
ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS
AB LY303366 is a novel semisynthetic derivative of **echinocandin** B and a potent inhibitor of fungal

PAGE 1-A



PAGE 2-A



REFERENCE COUNT: 18 THERE ARE 18 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L31 ANSWER 9 OF 23 HCAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 1998:271684 HCAPLUS
DOCUMENT NUMBER: 129:38662
TITLE: Photoaffinity analog of the semisynthetic

Searcher : Shears 308-4994

8
Carb

	echinocandin LY303366: identification of echinocandin targets in Candida albicans
AUTHOR(S):	Radding, Jeffrey A.; Heidler, Steven A.; Turner, William W.
CORPORATE SOURCE:	Lilly Research Laboratories, Department of Infectious Disease Research, Eli Lilly and Co., Indianapolis, IN, 46285, USA
SOURCE:	Antimicrobial Agents and Chemotherapy (1998), 42(5), 1187-1194 CODEN: AMACCQ; ISSN: 0066-4804
PUBLISHER:	American Society for Microbiology
DOCUMENT TYPE:	Journal
LANGUAGE:	English

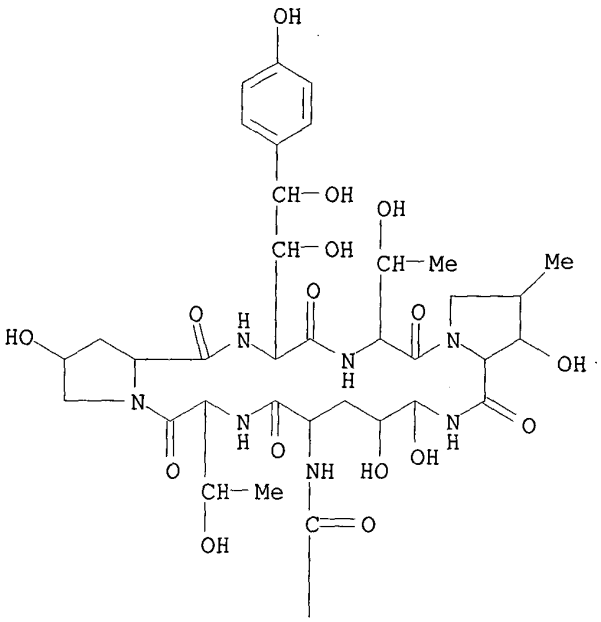
AB The echinocandins are a family of cyclic lipopeptides with potent antifungal activity. These compds. inhibit the synthesis of .beta.-1,3-glucan in fungi. The new semisynthetic echinocandin LY303366 was derivatized to produce a photoactivatable crosslinking echinocandin analog with antifungal activity. This analog was radioiodinated and used as a probe in microsomal membrane prepns. of Candida albicans which contain glucan synthase activity. The photoaffinity probe identified two major proteins of 40 and 18 kDa in both membrane prepns. Labeling of these proteins was specific in that it required irradn. with UV light and was effectively competed against with unlabeled echinocandin analogs. In addn., the abilities of echinocandin analogs to compete with the photoaffinity probe correlated to their relative antifungal potencies and glucan synthase inhibition. The 40-kDa protein was isolated, and partial sequences were obtained from internal peptide fragments of the protein. Anal. of the sequences of these internal peptides of the 40-kDa protein revealed that it was a new protein not previously described as being involved in glucan synthesis or the mode of action of echinocandins.

IT **166663-25-8**, LY303366
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)
(photoaffinity analog of semisynthetic echinocandin LY303366: identification of echinocandin targets in Candida albicans)

RN 166663-25-8 HCAPLUS

CN Echinocandin B, 1-[(4R,5R)-4,5-dihydroxy-N2-[[4''-(pentyloxy)[1,1':4',1''-terphenyl]-4-yl]carbonyl]-L-ornithine]- (9CI) (CA INDEX NAME)

PAGE 1-A



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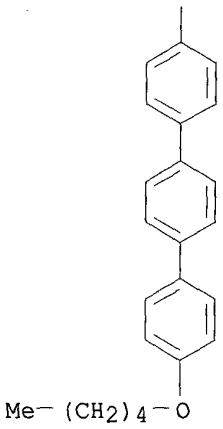


REFERENCE COUNT: 49 THERE ARE 49 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L31 ANSWER 10 OF 23 HCAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 1998:255543 HCAPLUS
DOCUMENT NUMBER: 129:187
TITLE: Efficacy of LY303366 against amphotericin

Searcher : Shears 308-4994

B-susceptible and -resistant Aspergillus fumigatus in a murine model of invasive aspergillosis

AUTHOR(S): Verweij, Paul E.; Oakley, Karen L.; Morrissey, Jacqui; Morrissey, Graham; Denning, David W.

CORPORATE SOURCE: Department of Medical Microbiology, University Hospital Nijmegen, Nijmegen, 6500 HB, Neth.

SOURCE: Antimicrobial Agents and Chemotherapy (1998), 42(4), 873-878
CODEN: AMACCQ; ISSN: 0066-4804

PUBLISHER: American Society for Microbiology

DOCUMENT TYPE: Journal

LANGUAGE: English

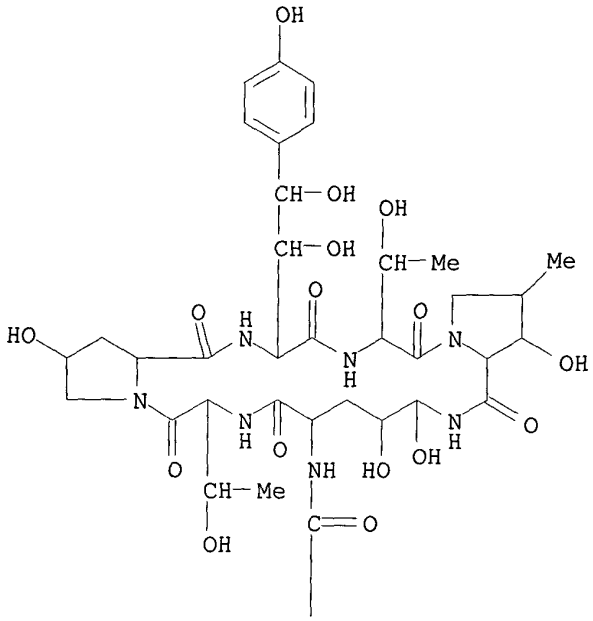
AB LY303366 is a novel antifungal echinocandin with excellent in vitro activity against Aspergillus spp. Four doses (1, 2.5, 10, and 25 mg/kg of body wt.) of LY303366 were compared with amphotericin B (0.5 to 5 mg/kg) in a temporarily neutropenic murine model of invasive aspergillosis against an amphotericin B-susceptible (AF210) and an amphotericin B-resistant (AF65) Aspergillus fumigatus isolate based on in vivo response. Mice were immunosuppressed with cyclophosphamide (200 mg/kg) and infected 3 days later. Treatment started 18 h after infection and lasted for 10 days. LY303366 was given once daily i.v. for 10 days, and amphotericin B (at 0.5, 2, and 5 mg/kg) was given once daily i.p. for 10 days, or only on days 1, 2, 4, and 7 (at 5 mg/kg). Kidneys and lungs from survivors were cultured on day 11. Control mice in both expts. had 90 to 100% mortality. Amphotericin B at 0.5 mg/kg and LY303366 at 1 mg/kg yielded 10 to 20% survival rates for mice infected with either AF210 or AF65. Amphotericin B at 2 and 5 (both regimens) mg/kg yielded a 70 to 100% survival rate for mice infected with AF210 but a 10 to 30% survival rate for mice infected with AF65 ($P = 0.01$ to 0.04 compared with AF210). Against AF210 and AF65, LY303366 at 2.5, 10, and 25 mg/kg produced a survival rate of 70 to 80%, which was as effective as amphotericin B for AF210, but superior to amphotericin B for AF65 ($P < 0.03$ to 0.0006). For AF65, LY303366 at 10 and 25 mg/kg/day was superior to amphotericin B at 2 and 5 mg/kg/day in reducing tissue colony counts ($P = 0.01$ to 0.003), and for AF210, amphotericin B at 5 mg/kg/day and at 5 mg/kg in four doses was more effective than all four regimens of LY303366 in reducing renal culture counts ($P = 0.01$ to 0.0001). The present study shows, for the first time, that in vivo resistance of A. fumigatus to amphotericin B exists, although this could not be detected by in vitro susceptibility assays. Furthermore, LY303366 appears to be effective against amphotericin B-susceptible and -resistant A. fumigatus infection in this model and should be further evaluated clin.

IT **166663-25-8**, LY303366
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)
(efficacy of LY303366 against amphotericin B-susceptible and -resistant Aspergillus fumigatus in a murine model of invasive aspergillosis)

RN 166663-25-8 HCAPLUS

CN Echinocandin B, 1-[(4R,5R)-4,5-dihydroxy-N2-[[4''-(pentyloxy)[1,1':4',1''-terphenyl]-4-yl]carbonyl]-L-ornithine]-(9CI) (CA INDEX NAME)

PAGE 1-A



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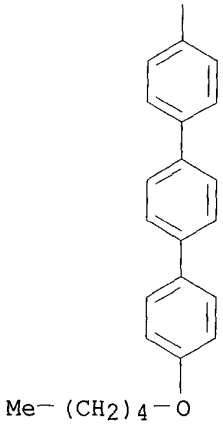


REFERENCE COUNT: 34 THERE ARE 34 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L31 ANSWER 11 OF 23 HCAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 1998:146172 HCAPLUS
DOCUMENT NUMBER: 128:243844
TITLE: The synthesis and antifungal activity of nitrogen containing hemiaminal ethers of

Searcher : Shears 308-4994

LY303366

AUTHOR(S): Jamison, James A.; Lagrandeur, Lisa M.; Rodriguez, Michael J.; Turner, William W.; Zeckner, Douglas J.

CORPORATE SOURCE: Infectious Diseases Research, Lilly Research Laboratories, Eli Lilly and Company, Indianapolis, IN, 46285, USA

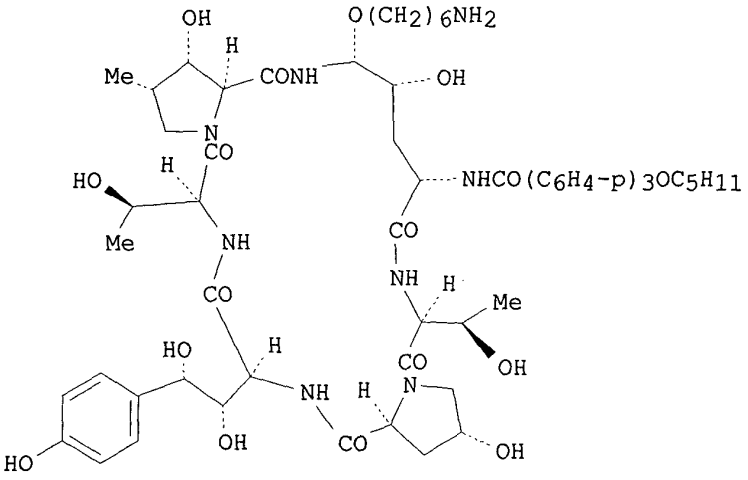
SOURCE: Journal of Antibiotics (1998), 51(2), 239-242
CODEN: JANTAJ; ISSN: 0021-8820

PUBLISHER: Japan Antibiotics Research Association

DOCUMENT TYPE: Journal

LANGUAGE: English

GI



I

AB The antifungal LY303366 reacted with amino alcs. and BOC protected alcs. in dioxane or DMSO to yield nitrogen contg. hemiaminal ethers, e.g. I. The hemiaminals with their increased chain length were evaluated for their antifungal properties and their MICs were compared to LY303366.

IT **166663-25-8**, LY303366
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); RCT (Reactant); BIOL (Biological study); RACT (Reactant or reagent)
(prepn. and antifungal activity of nitrogen contg. LY303366 hemiaminal ethers)

RN 166663-25-8 HCAPLUS

CN Echinocandin B, 1-[(4R,5R)-4,5-dihydroxy-N2-[[4''-(pentyloxy)[1,1':4',1''-terphenyl]-4-yl]carbonyl]-L-ornithine]- (9CI) (CA INDEX NAME)

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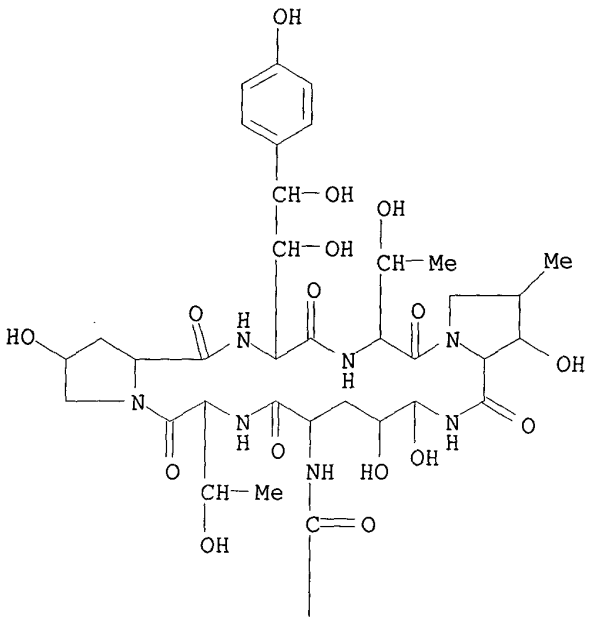

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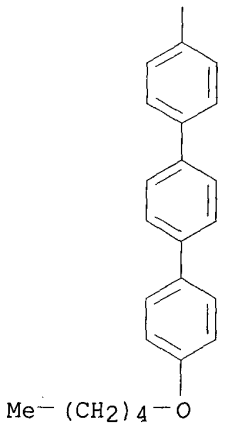


REFERENCE COUNT: 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L31 ANSWER 12 OF 23 HCAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 1998:49753 HCAPLUS
DOCUMENT NUMBER: 128:125716
TITLE: Growth medium effect on the antifungal activity

Searcher : Shears 308-4994

of LY 303366

AUTHOR(S): Klepser, Michael E.; Ernst, Erika J.; Ernst, Michael E.; Pfaller, Michael A.

CORPORATE SOURCE: College of Pharmacy, The University of Iowa, Iowa City, IA, 52242-1112, USA

SOURCE: Diagnostic Microbiology and Infectious Disease (1997), 29(4), 227-231
CODEN: DMIDDZ; ISSN: 0732-8893

PUBLISHER: Elsevier Science Inc.

DOCUMENT TYPE: Journal

LANGUAGE: English

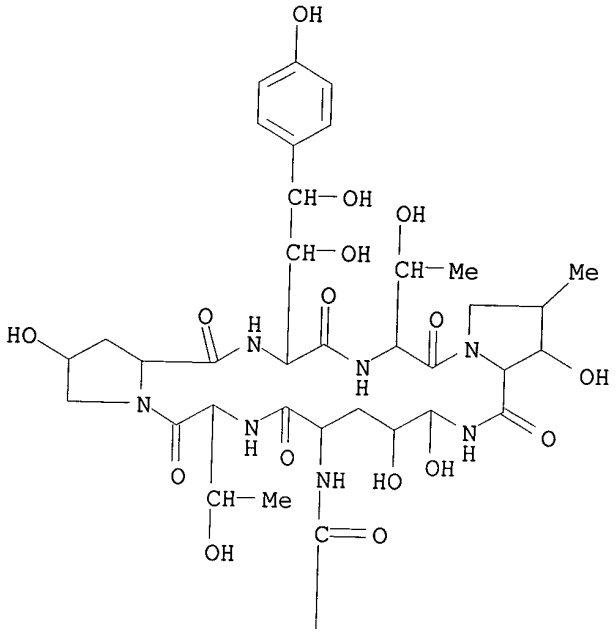
AB The impact of growth medium selection on antifungal susceptibility testing has been well documented. Previously, the authors described the antifungal characteristics of LY 303366 via time-kill curve methods using RPMI 1640 buffered with 0.165 M morpholinepropane-sulfonic acid as growth medium. The purpose of the current study was to compare the previously reported kill curve results with results obtained using antibiotic medium no. three (AM #3) as growth medium. Antifungal activity was assessed via susceptibility testing and time-kill studies in both media. Two isolates each of Candida albicans, C. glabrata, and C. tropicalis were studied. MICs for the six isolates were found to be 10 to 100 times lower in AM #3. Time-kill studies were conducted with multiples of the MIC ranging from 0.125 .times. MIC to 16 .times. MIC. LY 303366 exhibited fungicidal (.gtoreq.3 log10 redn. in CFU) activity against all isolates in AM #3; however, fungicidal activity was noted only for three of the six isolates when tested in RPMI. Furthermore, the rate of fungicidal activity was more rapid when AM #3 was utilized. Not only were the rate and extent of activity influenced by choice of media, but the relationships between LY 303366 concns. and activity were also found to be media dependent. The findings from this study serve to highlight further the importance of media selection for in vitro evaluation of antifungal activity. In vivo studies need to be conducted with LY 303366 to det. which media provides the best correlation between in vitro and in vivo findings.

IT **166663-25-8**, LY 303366
RL: BAC (Biological activity or effector, except adverse); BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(growth medium effect on antifungal activity of LY 303366)

RN 166663-25-8 HCAPLUS

CN Echinocandin B, 1-[(4R,5R)-4,5-dihydroxy-N2-[[4''-(pentyloxy)[1,1':4',1''-terphenyl]-4-yl]carbonyl]-L-ornithine]- (9CI) (CA INDEX NAME)

PAGE 1-A



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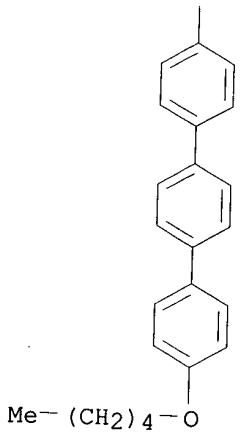
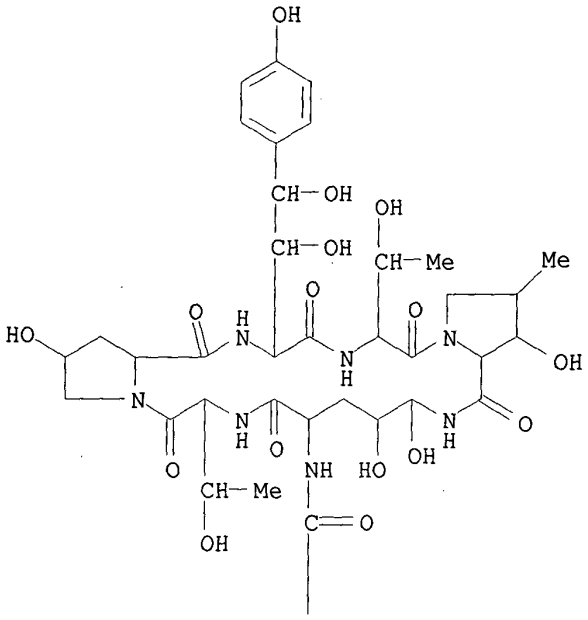


L31 ANSWER 13 OF 23 HCAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 1997:716937 HCAPLUS
DOCUMENT NUMBER: 127:343791
TITLE: In vitro kill curves of a new semisynthetic echinocandin, LY-303366, against fluconazole-sensitive and -resistant Candida species

Searcher : Shears 308-4994

AUTHOR(S): Karlowsky, James A.; Harding, Gary A. J.; Zelenitsky, Sheryl A.; Hoban, Daryl J.; Kabani, Amin; Balko, Tamara V.; Turik, Michael; Zhanel, George G.
CORPORATE SOURCE: Faculty Pharmacy, Department Medical Microbiology, Faculty Medicine, University Manitoba, Winnipeg, MB, Can.
SOURCE: Antimicrobial Agents and Chemotherapy (1997), 41(11), 2576-2578
CODEN: AMACCQ; ISSN: 0066-4804
PUBLISHER: American Society for Microbiology
DOCUMENT TYPE: Journal
LANGUAGE: English
AB In vitro killing by a new semisynthetic echinocandin, LY-303366, was characterized using clin. isolates of fluconazole-sensitive (Y58) and -resistant (Y180) Candida albicans as well as Candida glabrata (Y7) and Candida krusei (Y171). The 24-h kill curves for Y58 and Y180 demonstrated dose-independent killing of between 1 and 2 log10 with LY-303366 at concns. of 0.1, 1, 10, 50, 100, and 1000 times the MIC. Regrowth did not occur at 24 h with either C. albicans isolate at the aforementioned LY-303366 concns. At their MICs, LY-303366 and amphotericin B produced similar killing kinetics in cultures of Y58, Y180, Y7, and Y171, while all cultures exposed to fluconazole at its MIC demonstrated stasis or growth over 24 h.
IT **166663-25-8**, LY-303366
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)
(in vitro kill curves of new semisynthetic echinocandin, LY-303366, against fluconazole-sensitive and -resistant Candida species)
RN 166663-25-8 HCAPLUS
CN Echinocandin B, 1-[(4R,5R)-4,5-dihydroxy-N2-[[4''-(pentyloxy)[1,1':4',1''-terphenyl]-4-yl]carbonyl]-L-ornithine]- (9CI) (CA INDEX NAME)

PAGE 1-A



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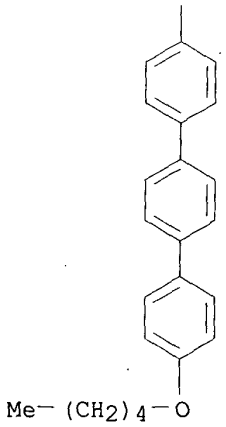


L31 ANSWER 14 OF 23 HCAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 1997:597380 HCAPLUS
DOCUMENT NUMBER: 127:275210
TITLE: Comparison of the in vitro activities of the echinocandin LY303366, the pneumocandin MK-0991, and fluconazole against Candida species and Cryptococcus neoformans

Searcher : Shears 308-4994

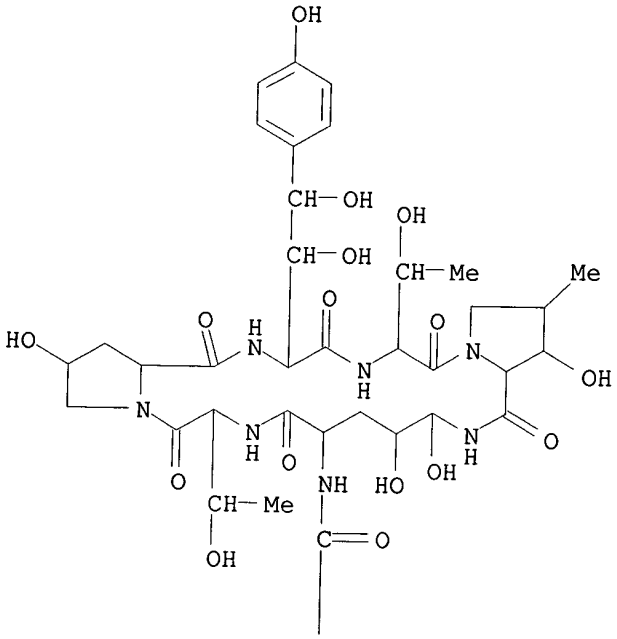
AUTHOR(S): Krishnarao, Tangella V.; Galgiani, John N.
CORPORATE SOURCE: Veterans Affairs Medical Center, Medical and Research Services, Tucson, AZ, 85723, USA
SOURCE: Antimicrobial Agents and Chemotherapy (1997), 41(9), 1957-1960
CODEN: AMACCQ; ISSN: 0066-4804
PUBLISHER: American Society for Microbiology
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Two new glucan synthesis inhibitors, the echinocandin LY303366 and the pneumocandin MK-0991 (formerly L-743,872), were studied for their antifungal activities in vitro in relation to each other and in relation to the activity of the triazole fluconazole. Systematic anal. of broth macrodiln. testing by varying the starting inoculum size, medium compn., medium pH, temp. of incubation, length of incubation, or selection of endpoints failed to identify significant differences in antifungal activity for either LY303366 or MK-0991 in comparison to the activity under std. test conditions specified for other antifungal agents in National Committee for Clin. Lab. Stds. (NCCLS) document M27A. Under standardized conditions, both drugs exhibited prominent activity against Candida spp., including C. glabrata and C. krusei, but showed little activity against Cryptococcus neoformans. This spectrum of activity differed from that of fluconazole, which exhibited marginal activity against C. glabrata and C. krusei but prominent activity against other Candida spp. and C. neoformans. For individual strains, broth microdiln. MICs of LY303366 and MK-0991 were similar to but frequently higher than broth macrodiln. results. In contrast, fluconazole broth microdiln. MICs were often lower than broth microdiln. results. The test conditions specified in NCCLS document M27A apparently are applicable to these 2 new glucan synthesis inhibitors; systematic differences between broth microdiln. procedures and the broth macrodiln. ref. std. will need to be addressed before the 2 test methods can be used interchangeably.

IT **166663-25-8**, LY303366
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)
(in vitro activities of the echinocandin LY303366, the pneumocandin MK-0991, and fluconazole against Candida species and Cryptococcus neoformans)

RN 166663-25-8 HCAPLUS
CN Echinocandin B, 1-[(4R,5R)-4,5-dihydroxy-N2-[[4''-(pentyloxy)[1,1':4',1''-terphenyl]-4-yl]carbonyl]-L-ornithine]- (9CI) (CA INDEX NAME)

PAGE 1-A



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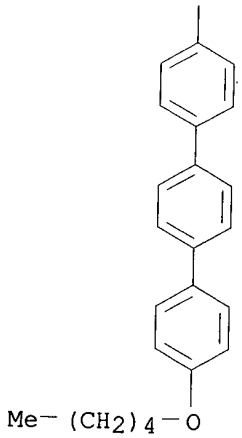


L31 ANSWER 15 OF 23 HCAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 1997:469681 HCAPLUS
DOCUMENT NUMBER: 127:185282
TITLE: Development of a plasma high-performance liquid chromatographic assay for LY303366, a lipopeptide antifungal agent, and its application in a dog pharmacokinetic study

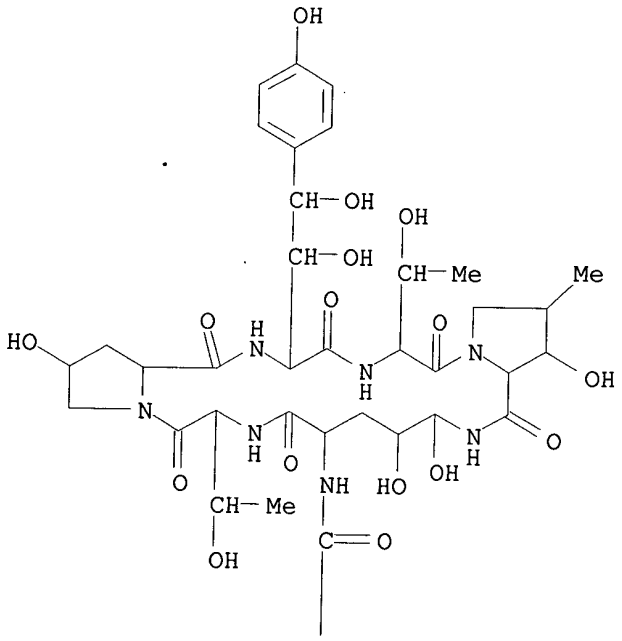
Searcher : Shears 308-4994

AUTHOR(S): Zornes, L. L.; Stratford, R. E.
CORPORATE SOURCE: Department of Pharmaceutical Sciences, Lilly Research Laboratories, Division of Eli Lilly and Company, Lilly Corporate Center, Indianapolis, IN, 46285, USA
SOURCE: Journal of Chromatography, B: Biomedical Sciences and Applications (1997), 695(2), 381-387
CODEN: JCBBEP; ISSN: 0378-4347
PUBLISHER: Elsevier
DOCUMENT TYPE: Journal
LANGUAGE: English
AB An HPLC assay for plasma anal. of LY303366 (I), a semi-synthetic lipopeptide antifungal related to echinocandin B (ECB), was developed to support the selection and subsequent preclin. development of I. The method involved extn. of I from plasma with the aid of solid-phase extn. (SPE) cartridges followed by reversed-phase HPLC with UV detection at 300 nm. The method is simple, selective and is applicable to dog, rat, mouse and rabbit plasma. Validation studies using dog plasma showed that the values obtained for parameters of linearity, precision and accuracy were within acceptable limits. Based on anal. of 0.3 mL of plasma, the lower limit of quantitation was 20 ng/mL. The method has been successfully applied to det. the pharmacokinetic parameters of I in the dog following i.v. and oral administration. Compared to first generation ECB antifungal agents, the results of the i.v. dog study indicated a 50% redn. in clearance of the drug from plasma (0.1 L/h/kg) and an 18-fold increase in the vol. of distribution at steady state (1.8 L/kg). When administered orally, compd. I had an abs. bioavailability of 9%; however, plasma levels remained above the MIC for C. albicans (0.005 .mu.g/mL) through 48 h. Given the excellent potency of I and its broad spectrum of activity relative to first generation ECB antifungal agents, the assay results for I indicate the potential for its use as a broad spectrum i.v. and oral antifungal agent.

IT **166663-25-8**, LY303366
RL: ANT (Analyte); BPR (Biological process); BSU (Biological study, unclassified); ANST (Analytical study); BIOL (Biological study); PROC (Process)
(development of HPLC assay for antifungal LY303366 in plasma in dog pharmacokinetic study)

RN 166663-25-8 HCAPLUS
CN Echinocandin B, 1-[(4R,5R)-4,5-dihydroxy-N2-[[4''-(pentyloxy)[1,1':4',1''-terphenyl]-4-yl]carbonyl]-L-ornithine]- (9CI) (CA INDEX NAME)

PAGE 1-A



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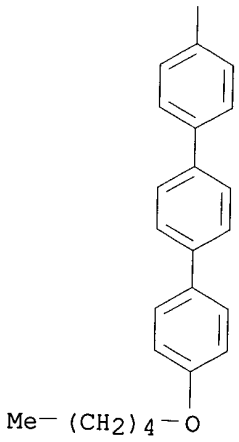


L31 ANSWER 16 OF 23 HCAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 1997:304710 HCAPLUS
DOCUMENT NUMBER: 127:15326
TITLE: In vitro activity of a new echinocandin, LY303366, compared with those of amphotericin B and fluconazole against clinical yeast isolates
AUTHOR(S): Uzun, Omrum; Kocagoz, Sesin; Cetinkaya, Yesim;

Searcher : Shears 308-4994

CORPORATE SOURCE: Arikan, Sevtap; Unal, Serhat
Sch. Med., Hacettepe Univ., Ankara, 06100, Turk.
SOURCE: Antimicrobial Agents and Chemotherapy (1997), 41(5), 1156-1157
CODEN: AMACCQ; ISSN: 0066-4804
PUBLISHER: American Society for Microbiology
DOCUMENT TYPE: Journal
LANGUAGE: English

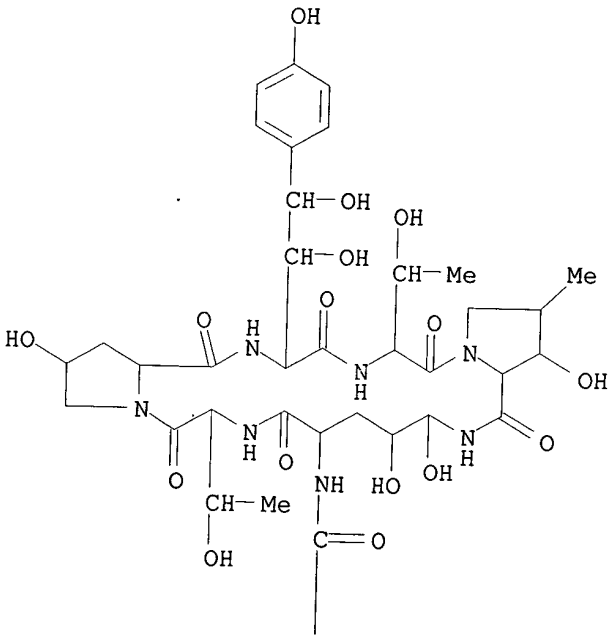
AB The in vitro activity of LY303366, a new echinocandin deriv., was evaluated with 191 yeast isolates by a broth microdilution method. The MICs at which 50% of the isolates were inhibited were 0.125 .mu.g/mL for Candida albicans and C. tropicalis, 0.25 .mu.g/mL for C. krusei, C. kefyr, and C. glabrata, and 2.0 .mu.g/mL for C. parapsilosis.

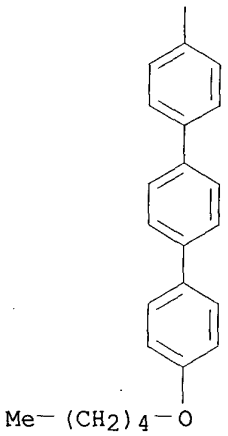
IT **166663-25-8**, LY303366
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)
(in vitro activity of LY303366, compared with amphotericin B and fluconazole, against clin. yeast isolates)

RN 166663-25-8 HCAPLUS

CN Echinocandin B, 1-[(4R,5R)-4,5-dihydroxy-N2-[[4''-(pentyloxy)[1,1':4',1''-terphenyl]-4-yl]carbonyl]-L-ornithine]-(9CI) (CA INDEX NAME)

PAGE 1-A





L31 ANSWER 17 OF 23 HCAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 1997:232724 HCAPLUS
DOCUMENT NUMBER: 126:290547
TITLE: In vitro activity of a new semisynthetic echinocandin, LY-303366, against systemic isolates of Candida species, Cryptococcus neoformans, Blastomyces dermatitidis, and Aspergillus species
AUTHOR(S): Zhanel, George G.; Karlowsky, James A.; Harding, Gary A. J.; Balko, Tamara V.; Zelenitsky, Sheryl A.; Friesen, Mark; Kabani, Amin; Turik, Michael; Hoban, Daryl J.
CORPORATE SOURCE: Department of Medical Microbiology, University of Manitoba, Winnipeg, MB, Can.
SOURCE: Antimicrobial Agents and Chemotherapy (1997), 41(4), 863-865
CODEN: AMACCQ; ISSN: 0066-4804
PUBLISHER: American Society for Microbiology
DOCUMENT TYPE: Journal
LANGUAGE: English

AB The in vitro activities of LY-303366, a new semisynthetic echinocandin, and comparators amphotericin B, 5-fluorocytosine, fluconazole, and ketoconazole against 205 systemic isolates of Candida species, Cryptococcus neoformans, Blastomyces dermatitidis, and Aspergillus species were detd. LY-303366 had MICs of .ltoreq.0.32 .mu.g/mL for all Candida albicans (n = 99), Candida glabrata (n = 18), and Candida tropicalis (n = 10) isolates tested. LY-303366 was also active against Aspergillus species (min. effective concn. at which 90% of the isolates are inhibited, 0.02 .mu.g/mL) (n = 20), was less active against Candida parapsilosis (MIC at which 90% of the isolates are inhibited [MIC90], 5.12 .mu.g/mL) (n = 10), and was inactive against C. neoformans (MIC90, > 10.24 .mu.g/mL) (n = 15) and B. dermatitidis (MIC90, 16 .mu.g/mL) (n = 29).

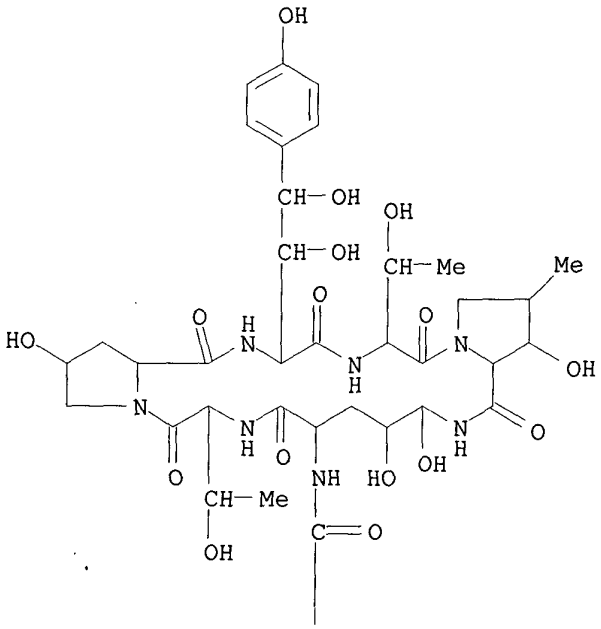
IT **166663-25-8**, LY-303366
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL

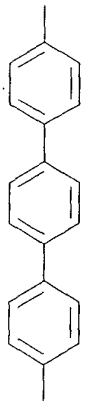
(Biological study); USES (Uses)
(in vitro activity of a new semisynthetic echinocandin, LY-303366, against systemic isolates of Candida species, Cryptococcus neoformans, Blastomyces dermatitidis, and Aspergillus species)

RN 166663-25-8 HCAPLUS

CN Echinocandin B, 1-[(4R,5R)-4,5-dihydroxy-N2-[[4''-(pentyloxy)[1,1':4',1''-terphenyl]-4-yl]carbonyl]-L-ornithine]-(9CI) (CA INDEX NAME)

PAGE 1-A





L31 ANSWER 18 OF 23 HCAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 1997:232701 HCAPLUS
DOCUMENT NUMBER: 126:290540
TITLE: In vitro susceptibilities of clinical yeast isolates to a new echinocandin derivative, LY303366, and other antifungal agents
AUTHOR(S): Pfaller, M. A.; Messer, S. A.; Coffman, S.
CORPORATE SOURCE: Department of Pathology, University of Iowa College of Medicine, Iowa City, IA, 52242, USA
SOURCE: Antimicrobial Agents and Chemotherapy (1997), 41(4), 763-766
CODEN: AMACCQ; ISSN: 0066-4804
PUBLISHER: American Society for Microbiology
DOCUMENT TYPE: Journal
LANGUAGE: English

AB LY303366 is a new semisynthetic echinocandin deriv. with potent, broad-spectrum fungicidal activity. We investigated the in vitro activity of LY303366, amphotericin B, flucytosine (5FC), fluconazole, and itraconazole against 435 clin. yeast isolates (413 Candida and 22 Saccharomyces cerevisiae isolates) obtained from over 30 different medical centers. MICs for all five antifungal agents were detd. by the National Committee for Clin. Lab. Stds. method with RPMI 1640 test medium. LY303366 was also tested in antibiotic medium 3 as specified by the manufacturer. Overall, LY303366 was quite active against all of the yeast isolates when tested in RPMI 1640 (MIC at which 90% of the isolates are inhibited [MIC90], 1.0 .mu.g/mL) but appeared to be considerably more potent when tested in antibiotic medium 3 (MIC90, 0.03 .mu.g/mL). When tested in antibiotic medium 3, LY303366 was 16- to >2,000-fold more active than itraconazole, fluconazole, amphotericin B, or 5FC against all species except Candida parapsilosis. When tested in RPMI 1640, LY303366 was comparable to amphotericin B and itraconazole and more active than fluconazole and 5FC. All of the isolates for which fluconazole and itraconazole had elevated MICs (.gtoreq.128 and .gtoreq.2.0 .mu.g/mL, resp.) were inhibited by .ltoreq.0.007 .mu.g of LY303366/mL when tested in antibiotic medium 3 and .ltoreq.0.5 .mu.g/mL when tested in RPMI 1640. Based on these studies, LY303366

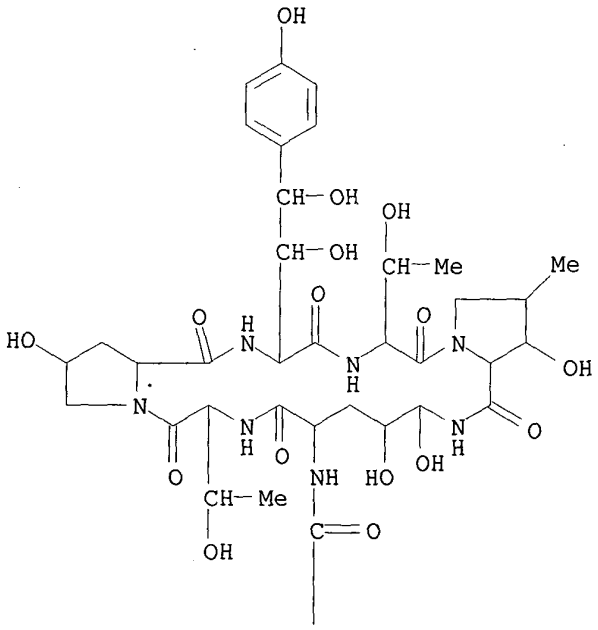
has promising antifungal activity and warrants further in vitro and in vivo investigation.

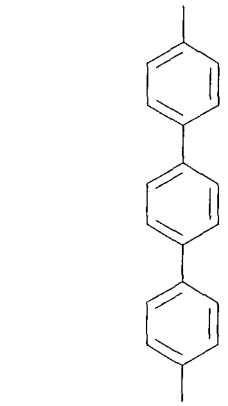
IT **166663-25-8**, LY303366
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(susceptibilities of clin. yeast isolates to a new echinocandin deriv., LY303366, and other antifungal agents)

RN 166663-25-8 HCAPLUS

CN Echinocandin B, 1-[(4R,5R)-4,5-dihydroxy-N2-[[4''-(pentyloxy)[1,1':4',1''-terphenyl]-4-yl]carbonyl]-L-ornithine]- (9CI) (CA INDEX NAME)

PAGE 1-A





L31 ANSWER 19 OF 23 HCAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 1997:222834 HCAPLUS
DOCUMENT NUMBER: 126:258551
TITLE: Antifungal dynamics of LY 303366, an investigational echinocandin B analog, against Candida ssp
AUTHOR(S): Ernst, Michael E.; Klepser, Michael E.; Wolfe, Erika J.; Pfaller, Michael A.
CORPORATE SOURCE: Colleges of Pharmacy, The University of Iowa, Iowa, IA, 52242-1112, USA
SOURCE: Diagnostic Microbiology and Infectious Disease (1996), 26(3/4), 125-131
CODEN: DMIDDZ; ISSN: 0732-8893
PUBLISHER: Elsevier
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Two isolates each of Candida albicans, Candida tropicalis, and Candida glabrata were selected for time-kill curve testing against LY 303366 at concns. ranging from 0.125 .times. MIC to 16 .times. MIC. RPMI 1640 buffered with morpholinepropanesulfonic acid (MOPS) was utilized as growth medium. Samples were obtained at predetd. time points over 24 h and streaked for colony count detn. Against C. albicans (one strain) and C. glabrata isolates, LY 303366 exhibited fungicidal (.gtoreq.three log10 redn. in CFU) activity. In contrast, fungistatic activity was obsd. with LY 303366 against C. albicans (one strain) and C. tropicalis isolates at all of the multiples of the MIC tested. With the exception of one C. glabrata strain, the rate and extent of activity against test isolates was not enhanced with concns. exceeding the MIC. Our data indicate that maximal antifungal activity with LY 303366 may be achieved by optimizing the time of fungal exposure to the drug. Addnl., these data suggest that use of the current interpretive endpoint for MICs in RPMI may underestimate the antifungal activity of LY 303366. Thus, the MIC endpoint may need to be re-evaluated, or perhaps an alternative media, such as antibiotic medium #3, should be utilized for detn. of LY 303366 MICs.

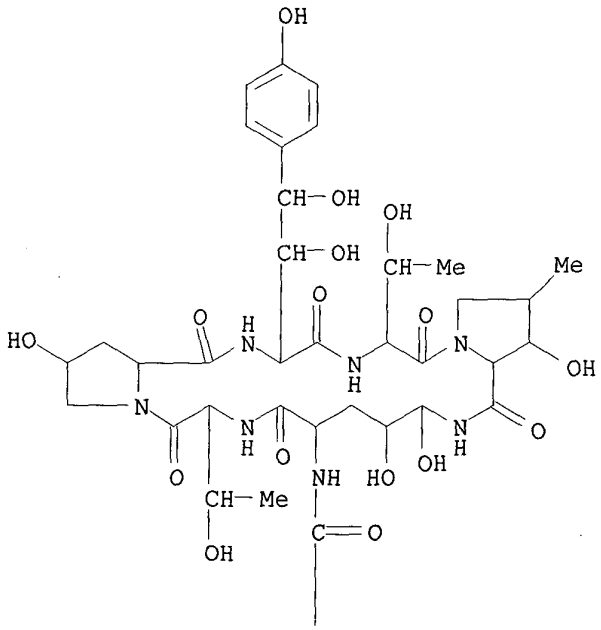
IT **166663-25-8**, LY 303366

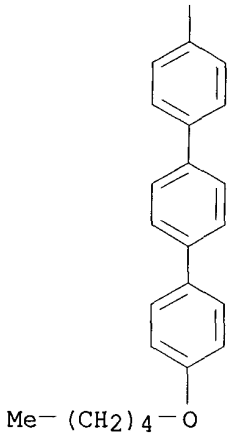
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(antifungal dynamics of LY 303366, an investigational echinocandin B analog, against Candida species)

RN 166663-25-8 HCAPLUS

CN Echinocandin B, 1-[(4R,5R)-4,5-dihydroxy-N2-[[4''-(pentyloxy)[1,1':4',1''-terphenyl]-4-yl]carbonyl]-L-ornithine]-(9CI) (CA INDEX NAME)

PAGE 1-A





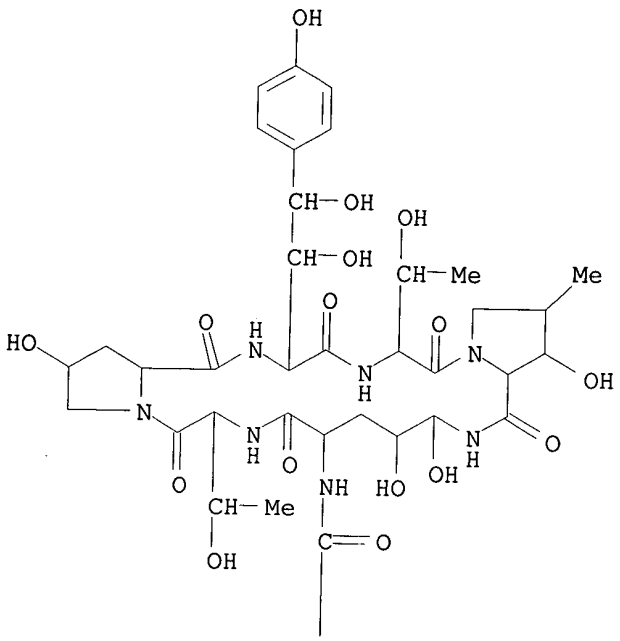
L31 ANSWER 20 OF 23 HCAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 1996:469901 HCAPLUS
DOCUMENT NUMBER: 125:211861
TITLE: Semisynthetic echinocandins affect cell wall deposition of Pneumocystis carinii in vitro and in vivo
AUTHOR(S): Bartlett, Marilyn S.; Current, William L.; Goheen, Michael P.; Boylan, Carole J.; Lee, Chao H.; Shaw, Margaret M.; Queener, Sherry F.; Smith, James W.
CORPORATE SOURCE: Dep. Pathology Pharmacology Toxicology, Indiana Univ., Indianapolis, IN, USA
SOURCE: Antimicrobial Agents and Chemotherapy (1996), 40(8), 1811-1816
CODEN: AMACCQ; ISSN: 0066-4804
PUBLISHER: American Society for Microbiology
DOCUMENT TYPE: Journal
LANGUAGE: English

AB A semisynthetic, water-sol. echinocandin analog, LY 307853, is effective in reducing the nos. of all life cycle forms of P. carinii and is more effective in mice immunosuppressed with monoclonal antibody to L3T4+ cells than in mice immunosuppressed with dexamethasone was demonstrated. Treatment of P. carinii isolates with LY 307853 in a short-term in vitro culture model resulted in cyto-architectural alterations suggesting that this echinocandin may interfere with the export of surface glycoprotein and the formation of the tubular elements normally found on the surfaces of trophic forms. The cyto-architectural changes in trophic forms treated in vitro with LY 307853 were also obsd. in trophic forms in the lung tissue of rats treated with a closely related echinocandin analog, LY 303366.

IT **166663-25-8**, LY 303366
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(semisynthetic echinocandins affect cell wall deposition of Pneumocystis carinii in vitro and in vivo)

RN 166663-25-8 HCAPLUS
CN Echinocandin B, 1-[(4R,5R)-4,5-dihydroxy-N2-[[4''-(pentyloxy)[1,1':4',1''-terphenyl]-4-yl]carbonyl]-L-ornithine]-(9CI) (CA INDEX NAME)

PAGE 1-A



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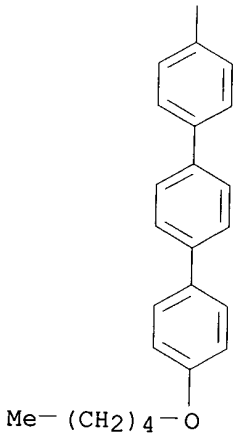


L31 ANSWER 21 OF 23 HCAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 1996:451996 HCAPLUS

DOCUMENT NUMBER: 125:143309
TITLE: Preparation of aza cyclohexapeptide compounds as antifungal agents for the treatment of Pneumocystis carinii infections
INVENTOR(S): Balkovec, James M.; Bouffard, Frances A.; Dropinski, James F.
PATENT ASSIGNEE(S): Merck and Co., Inc., USA
SOURCE: PCT Int. Appl., 70 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9608507	A1	19960321	WO 1995-US11541	19950912
W: AM, AU, BB, BG, BR, BY, CA, CN, CZ, EE, FI, GE, HU, IS, JP, KG, KR, KZ, LK, LR, LT, LV, MD, MG, MK, MN, MX, NO, NZ, PL, RO, RU, SG, SI, SK, TJ, TM, TT, UA, UG, US, UZ				
RW: KE, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
US 5514651	A	19960507	US 1994-307978	19940916
AU 9535512	A1	19960329	AU 1995-35512	19950912
PRIORITY APPLN. INFO.:			US 1994-307978	19940916
			WO 1995-US11541	19950912

OTHER SOURCE(S): MARPAT 125:143309
GI

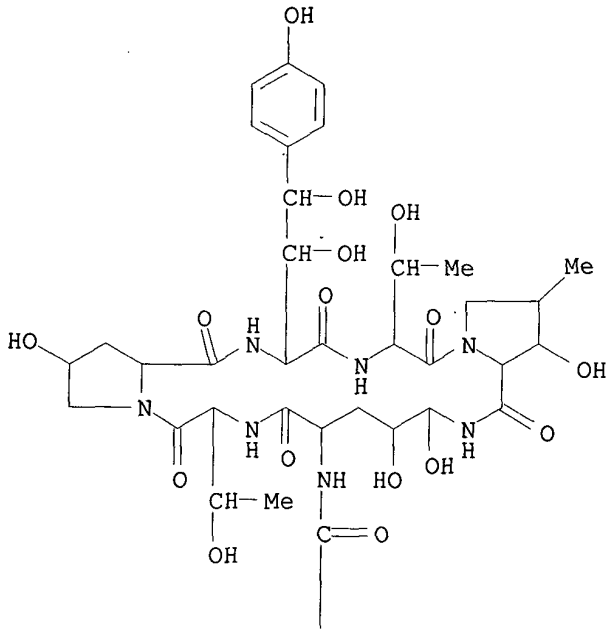
* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

AB The title compds. [I; R1 = Me, CH2CN, CH2CH2CN, CH2CONH2; R2 = H, Me, OH; R3 = Q; wherein p = 1,2,3; Ra = C1-10 alkyl, (CH2)qNRbRc (q = 2,3,4); wherein Ra, Rb = H, C1-10; or N RaRb = 4-C1-16 alkyl-, 4-phenyl-, or 4-benzyl-1-piperidinyl or -piperazinyl; R4 = H, C1-4 alkyl, C3-4 alkenyl, (CH2)2-4-OH, CO(CH2)1-4-NH2, optionally N-C1-4 alkylated (CH2)2-4-NH2; R5 = H, C1-4 alkyl; or R4R5 = (CH2)4, (CH2)5, CH2CH2OCH2CH2, CH2CH2NHCH2CH2], useful as antifungal agents and for the treatment of Pneumocystis carinii infections (no data), are prepd. Thus, an mixt. of a sulfone (II; R = H2NCH2CH2SO2) and its epimer (prepn. given) was stirred with ethylene diamine in DMF at room temp. for 1-12 h to give the desired product with the .alpha.-C-5 ornithine configuration II (R = H2NCH2CH2NH) (III) and its .beta.-C-5 epimer. Each tablet and gelatin capsule formulation, aerosol compn., and injectable soln. contg. III were formulated.

IT **166663-25-8**
RL: RCT (Reactant); RACT (Reactant or reagent)
(prepn. of aza cyclohexapeptide compds. as antifungal agents for treatment of Pneumocystis carinii infections)

RN 166663-25-8 HCAPLUS
CN Echinocandin B, 1-[(4R,5R)-4,5-dihydroxy-N2-[[4''-(pentyloxy)[1,1':4',1''-terphenyl]-4-yl]carbonyl]-L-ornithine]- (9CI) (CA INDEX NAME)

PAGE 1-A



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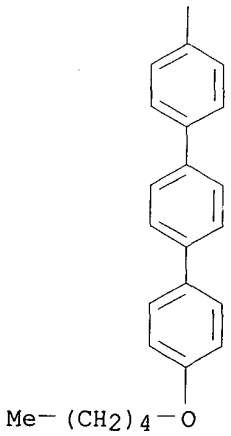


L31 ANSWER 22 OF 23 HCAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 1995:996828 HCAPLUS
DOCUMENT NUMBER: 124:146869
TITLE: Preparation of cyclopeptide antifungal and anti-pneumocystis compounds.
INVENTOR(S): Balkovec, James M.; Bouffard, Frances Aileen; Black, Regina M.

Searcher : Shears 308-4994

PATENT ASSIGNEE(S): Merck and Co., Inc., USA
SOURCE: PCT Int. Appl., 81 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9527074	A1	19951012	WO 1995-US3948	19950331
W: AM, AU, BB, BG, BR, BY, CA, CN, CZ, EE, FI, GE, HU, IS, JP, KG, KR, KZ, LK, LR, LT, LV, MD, MG, MN, MX, NO, NZ, PL, RO, RU, SG, SI, SK, TJ, TT, UA, UZ				
RW: KE, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
US 5541160	A	19960730	US 1994-222157	19940404
AU 9521307	A1	19951023	AU 1995-21307	19950331
PRIORITY APPLN. INFO.:			US 1994-222157	19940404
			WO 1995-US3948	19950331

OTHER SOURCE(S): MARPAT 124:146869
GI

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

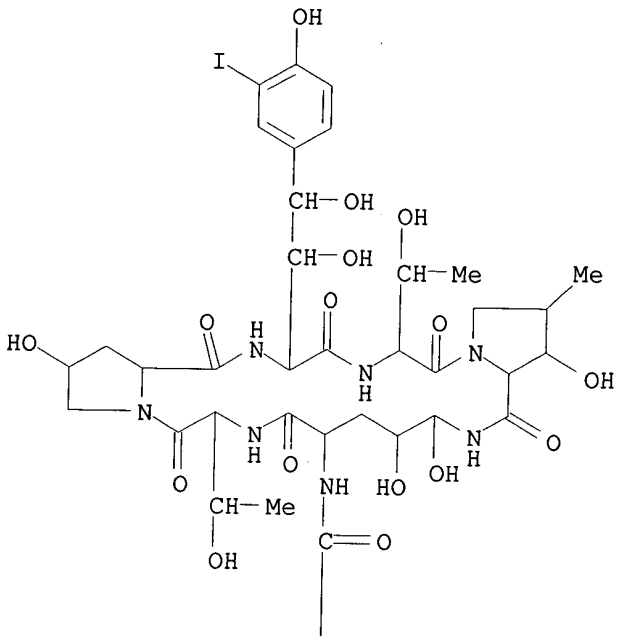
AB Title compds. [I; R = alkyl, alkenyl, Ph, biphenyl, naphthyl, terphenyl, alkylamino, dialkylamino, alkoxyaryl; R1, R2, R4 = H, OH; R3 = H, OH, O(CH2)nNRVRVI (RV, RVI, RVII = H, alkyl), O(CH2)nNRVRVIRVII+Y-; n = 2-6; Y = counterion; R5 = H, Me, OH; R6 = H, Me; R7 = H, Me, CH2C(:O)NH2, (CH2)2NRVRVI, (CH2)2NRVRVIRVII+Y-; R8 = Cl, Br, iodo, NO2, N3, (CH2)0-4NH2, (CH2)0-4NHalkyl, (CH2)0-4N(alkyl)2, (CH2)0-3CH(:NOH), NHC(:O)(CH2)1-6NH2, NHC(:O)(CH2)1-6NHC(:NH)(CH2)0-3H], were prepd. Thus, title compd. (II) (prepd. from pneumocandin B0) showed a min. fungicidal concn. of 0.25 .mu.g/mL against Candida albicans MY1055.

IT **173305-76-5P 173305-82-3P 173305-83-4P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of cyclopeptide antifungal and anti-pneumocystis compds.)

RN 173305-76-5 HCAPLUS

CN Echinocandin B, 1-[(4R,5R)-4,5-dihydroxy-N2-[[4''-(pentyloxy)[1,1':4',1''-terphenyl]-4-yl]carbonyl]-L-ornithine]-4-[(S)-4-hydroxy-4-(4-hydroxy-3-iodophenyl)-L-threonine]- (9CI) (CA INDEX NAME)

PAGE 1-A



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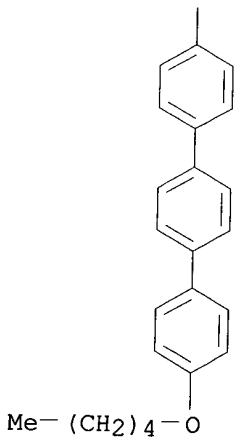
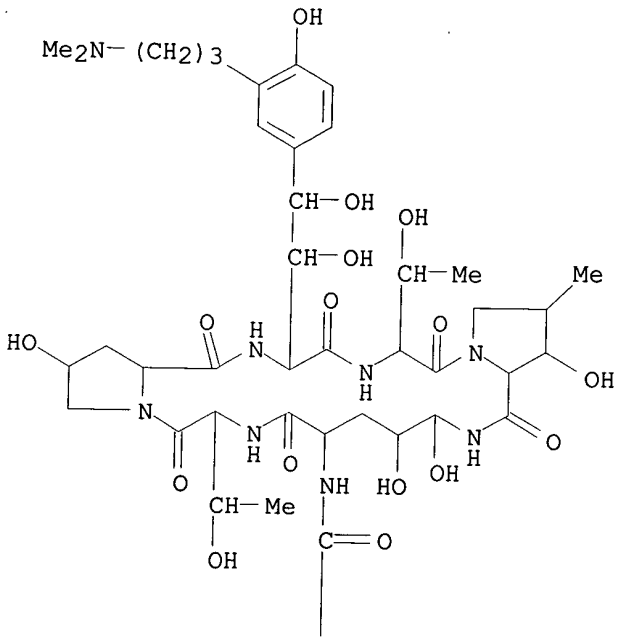


RN 173305-82-3 HCAPLUS
CN Echinocandin B, 1-[(4R,5R)-4,5-dihydroxy-N2-[[4''-(pentyloxy)[1,1':4',1''-terphenyl]-4-yl]carbonyl]-L-ornithine]-4-[4-[3-[3-(dimethylamino)propyl]-4-hydroxyphenyl]-(S)-4-hydroxy-L-threonine]- (9CI) (CA INDEX NAME)

PAGE 1-A



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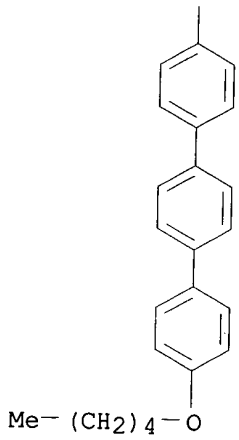

RN 173305-83-4 HCAPLUS
CN Echinocandin B, 1-[(4R,5R)-4,5-dihydroxy-N2-[[4''-(pentyloxy)[1,1':4',1''-terphenyl]-4-yl]carbonyl]-L-ornithine]-4-[(S)-4-hydroxy-4-[4-hydroxy-3-[3-(hydroxyimino)propyl]phenyl]-L-threonine]- (9CI) (CA INDEX NAME)

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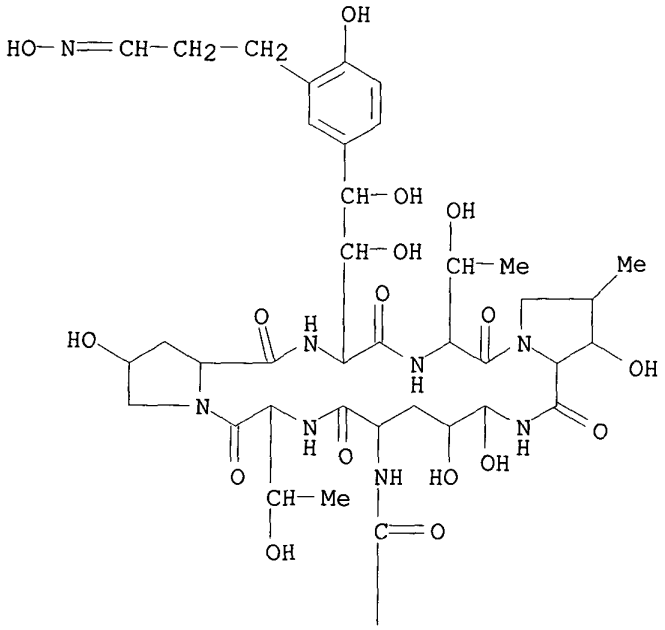

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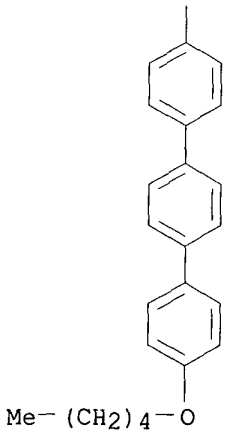
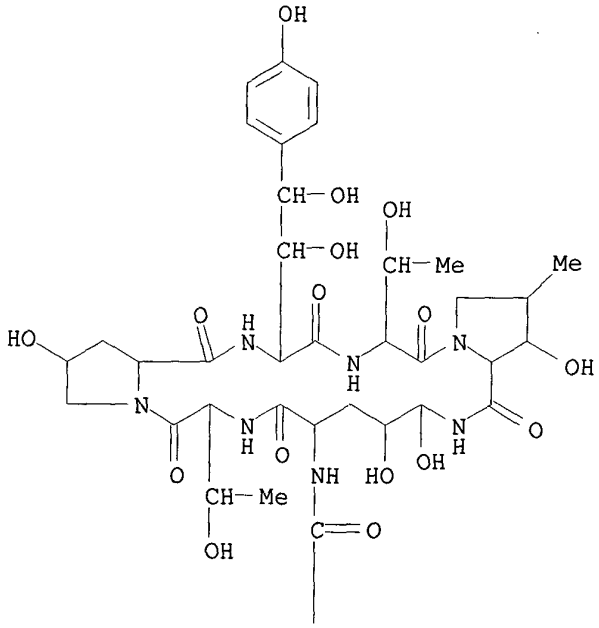


IT **166663-25-8P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(prepn. of cyclopeptide antifungal and anti-pneumocystis compds.)
RN 166663-25-8 HCAPLUS
CN Echinocandin B, 1-[(4R,5R)-4,5-dihydroxy-N2-[[4''-(pentyloxy)[1,1':4',1''-terphenyl]-4-yl]carbonyl]-L-ornithine]- (9CI) (CA INDEX NAME)

PAGE 1-A



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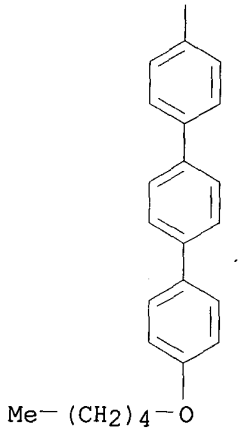


L31 ANSWER 23 OF 23 HCAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 1995:726672 HCAPLUS
DOCUMENT NUMBER: 123:160071
TITLE: Semisynthetic Chemical Modification of the Antifungal Lipopeptide Echinocandin B (ECB): Structure-Activity Studies of the Lipophilic and

Geometric Parameters of Polyarylated Acyl Analogs of ECB

AUTHOR(S): Debono, Manuel; Turner, William W.; LaGrandeur, Lisa; Burkhardt, Fred J.; Nissen, Jeffrey S.; Nichols, Kimberly K.; Rodriguez, Michael J.; Zweifel, Mark J.; Zeckner, Douglas J.; et al.

CORPORATE SOURCE: Lilly Research Laboratories, Eli Lilly and Company Inc., Indianapolis, IN, 46285, USA

SOURCE: Journal of Medicinal Chemistry (1995), 38(17), 3271-81
CODEN: JMCMAR; ISSN: 0022-2623

PUBLISHER: American Chemical Society

DOCUMENT TYPE: Journal

LANGUAGE: English

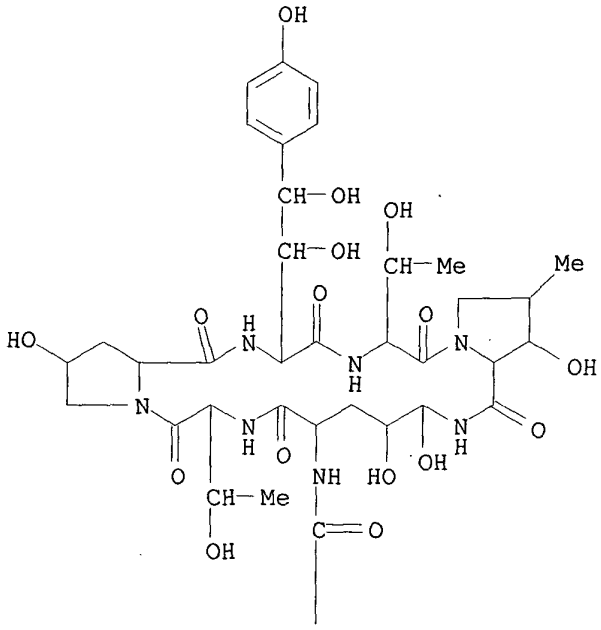
AB Echinocandin B (ECB) is a lipopeptide composed of a complex cyclic peptide acylated at the N-terminus by linoleic acid. Enzymic deacylation of ECB provided the peptide "nucleus" as a biol. inactive substrate from which novel ECB analogs were generated by chem. reacylation at the N-terminus. Varying the acyl group revealed that the structure and phys. properties of the side chain, particularly its geometry and lipophilicity, played a pivotal role in detg. the antifungal potency properties of the analog. Using CLOGP values to describe and compare the lipophilicities of the side chain fragments, it was shown that values of >3.5 were required for expression of antifungal activity. Secondly, a linearly rigid geometry of the side chain was the most effective shape in enhancing the antifungal potency. Using these parameters as a guide, a variety of novel ECB analogs were synthesized which included arylacyl groups that incorporated biphenyl, terphenyl, tetra-Ph, and arylethynyl groups. Generally the glucan synthase inhibition by these analogs correlated well with in vitro and in vivo activities and was likewise influenced by the structure of the side chain. These structural variations resulted in enhancement of antifungal activity in both in vitro and in vivo assays. Some of these analogs, including LY303366, were effective by the oral route of administration.

IT **166663-25-8P 166663-26-9P 166663-27-0P 166663-28-1P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); PRP (Properties); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(structure-activity studies of the lipophilic and geometric parameters of polyarylated acyl analogs of antifungal lipopeptide echinocandin B)

RN 166663-25-8 HCAPLUS

CN Echinocandin B, 1-[(4R,5R)-4,5-dihydroxy-N2-[[4''-(pentyloxy)[1,1':4',1''-terphenyl]-4-yl]carbonyl]-L-ornithine]- (9CI) (CA INDEX NAME)

PAGE 1-A



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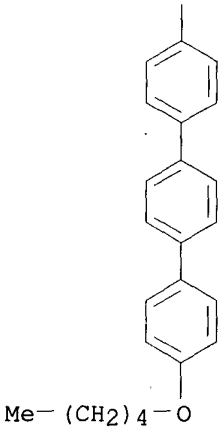
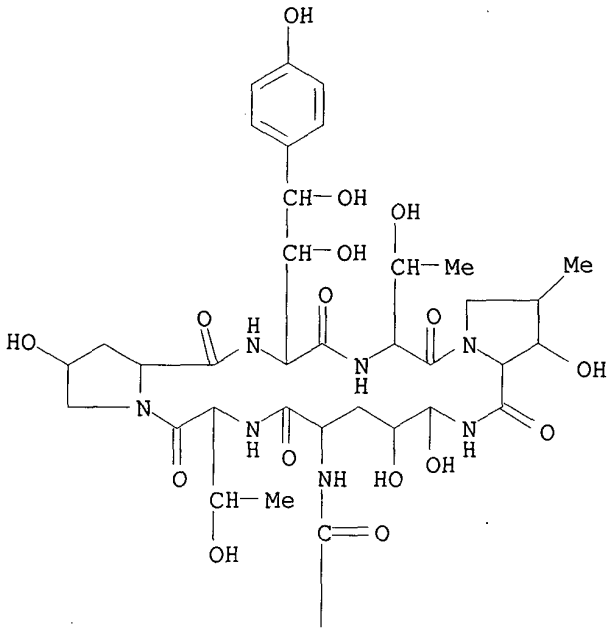


RN 166663-26-9 HCAPLUS
CN Cilofungin, 1-[(4R,5R)-N2-[[4''-(hexyloxy)[1,1':4',1''-terphenyl]-4-yl]carbonyl]-4,5-dihydroxy-L-ornithine]- (9CI) (CA INDEX NAME)

PAGE 1-A



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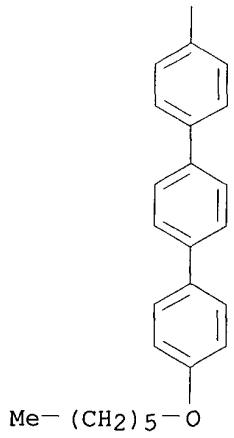
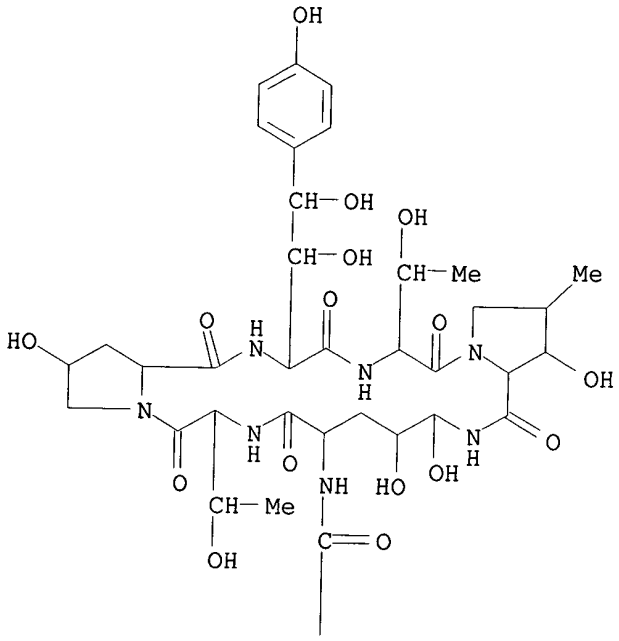


RN 166663-27-0 HCAPLUS
CN Echinocandin B, 1-[N2-[[4''-[(5-butoxypentyl)oxy][1,1':4',1''-terphenyl]-4-yl]carbonyl]-(4R,5R)-4,5-dihydroxy-L-ornithine]- (9CI) (CA INDEX NAME)

PAGE 1-A



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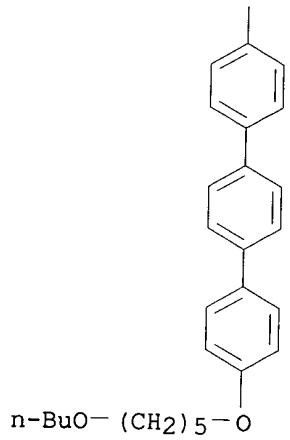

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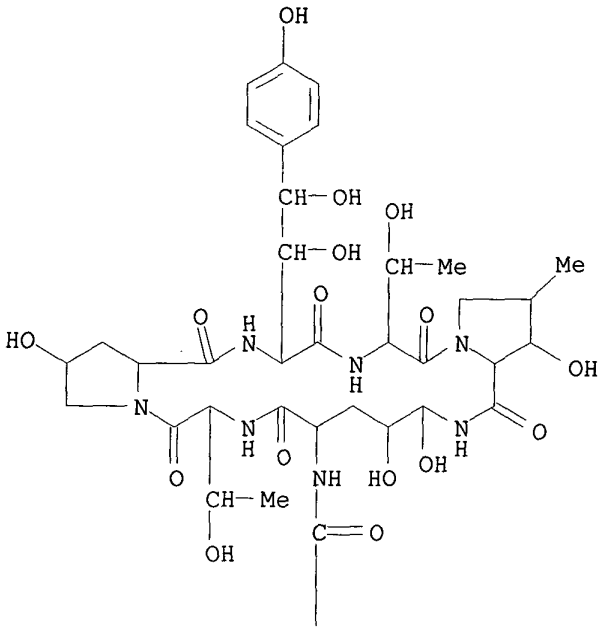
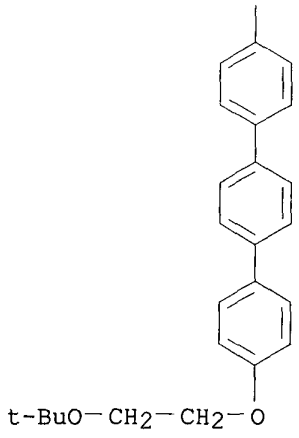
PAGE 1-A



PAGE 2-A



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L33 0 S L32

Searcher : Shears 308-4994

FILE 'USPATFULL' ENTERED AT 15:05:29 ON 06 JUN 2003
L34 14 S L32

L34 ANSWER 1 OF 14 USPATFULL

ACCESSION NUMBER:	2003:45293 USPATFULL
TITLE:	EDTA and other chelators with or without antifungal antimicrobial agents for the prevention and treatment of fungal infections
INVENTOR(S):	Raad, Issam, Houston, TX, UNITED STATES Sherertz, Robert, Winston-Salem, NC, UNITED STATES Hachem, Ray, Houston, TX, UNITED STATES
PATENT ASSIGNEE(S):	Board of Regents, The University of Texas System (U.S. corporation)

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 2003032605	A1	20030213
APPLICATION INFO.:	US 2002-254430	A1	20020925 (10)

RELATED APPLN. INFO.: Continuation of Ser. No. US 2000-680061, filed on 4 Oct 2000, PENDING Continuation of Ser. No. US 1998-139522, filed on 25 Aug 1998, GRANTED, Pat. No. US 6165484

	NUMBER	DATE
PRIORITY INFORMATION:	US 1997-56970P	19970826 (60)

DOCUMENT TYPE:	Utility
FILE SEGMENT:	APPLICATION
LEGAL REPRESENTATIVE:	David L. Parker, FULBRIGHT & JAWORSKI L.L.P., 600 Congress Avenue, Suite 2400, Austin, TX, 78701
NUMBER OF CLAIMS:	28
EXEMPLARY CLAIM:	1
NUMBER OF DRAWINGS:	11 Drawing Page(s)
LINE COUNT:	1420

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB A pharmaceutical composition comprising at least one antifungal agent and at least one chelator, and a method for administering the pharmaceutical composition to a patient having a fungal infection. Another aspect provides a pharmaceutical composition comprising at least one chelator, at least one antifungal agent and at least one monoclonal antibody, wherein the monoclonal antibody is operatively attached to the chelator, and a method of administering this composition to a patient having a fungal infection.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L34 ANSWER 2 OF 14 USPATFULL

ACCESSION NUMBER:	2003:20215 USPATFULL
TITLE:	EDTA and other chelators with or without antifungal antimicrobial agents for the prevention and treatment of fungal infections
INVENTOR(S):	Raad, Issam, Houston, TX, United States Sherertz, Robert, Winston-Salem, NC, United States Hachem, Ray, Houston, TX, United States
PATENT ASSIGNEE(S):	Board of Regents, The University of Texas System,

Austin, TX, United States (U.S. corporation)

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 6509319	B1	20030121
APPLICATION INFO.:	US 2000-680061		20001004 (9)
RELATED APPLN. INFO.:	Continuation of Ser. No. US 1998-139522, filed on 25 Aug 1998, now patented, Pat. No. US 6165484		

	NUMBER	DATE
PRIORITY INFORMATION:	US 1997-56970P	19970826 (60)

DOCUMENT TYPE: Utility
FILE SEGMENT: GRANTED
PRIMARY EXAMINER: Peselev, Elli
LEGAL REPRESENTATIVE: Fulbright & Jaworski
NUMBER OF CLAIMS: 16
EXEMPLARY CLAIM: 1,9
NUMBER OF DRAWINGS: 11 Drawing Figure(s); 11 Drawing Page(s)
LINE COUNT: 1664
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB A pharmaceutical composition comprising at least one antifungal agent and at least one chelator, and a method for administering the pharmaceutical composition to a patient having a fungal infection. Another aspect provides a pharmaceutical composition comprising at least one chelator, at least one antifungal agent and at least one monoclonal antibody, wherein the monoclonal antibody is operatively attached to the chelator, and a method of administering this composition to a patient having a fungal infection.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L34 ANSWER 3 OF 14 USPATFULL
ACCESSION NUMBER: 2002:317494 USPATFULL
TITLE: Cyclic compounds
INVENTOR(S): Aoki, Masahiro, Chigasaki, JAPAN
Kohchi, Masami, Fujisawa, JAPAN
Masubuchi, Kazunao, Yokohama, JAPAN
Mizuguchi, Eisaku, Kamakura, JAPAN
Murata, Takeshi, Chigasaki, JAPAN
Ohkuma, Hiroaki, Tokyo, JAPAN
Okada, Takehiro, Fujisawa, JAPAN
Sakaitani, Masahiro, Chigasaki, JAPAN
Shimma, Nobuo, Chigasaki, JAPAN
Watanabe, Takahide, Kamakura, JAPAN
Yanagisawa, Mieko, Yokohama, JAPAN
Yasuda, Yuri, Chigasaki, JAPAN
PATENT ASSIGNEE(S): Basilea Pharmaceutica AG, Binningen, SWITZERLAND (non-U.S. corporation)

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 6489440	B1	20021203
APPLICATION INFO.:	US 1999-360476		19990723 (9)

	NUMBER	DATE

PRIORITY INFORMATION: EP 1998-113744 19980723
EP 1999-107637 19990416
DOCUMENT TYPE: Utility
FILE SEGMENT: GRANTED
PRIMARY EXAMINER: Low, Christopher S. F.
ASSISTANT EXAMINER: Lukton, David
LEGAL REPRESENTATIVE: Johnston, George W., Tramaloni, Dennis P.
NUMBER OF CLAIMS: 51
EXEMPLARY CLAIM: 1
NUMBER OF DRAWINGS: 11 Drawing Figure(s); 11 Drawing Page(s)
LINE COUNT: 2791
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB The present invention relates to novel Aerothricins represented by the Formula (I), ##STR1##

wherein R.sup.1, R.sup.2, R.sup.3, R.sup.4, R.sup.5, X, Y, Z, and m are as defined in Claim 1; and pharmaceutically acceptable salts thereof.

The present invention also relates to a pharmaceutical composition comprising an Aerothricin of the Formula (I) and a pharmaceutically acceptable carrier. Furthermore, the present invention relates to the use of such Aerothricins for the preparation of medicaments, as well as to processes and intermediates for the preparation of the Aerothricins of the Formula (I).

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L34 ANSWER 4 OF 14 USPATFULL
ACCESSION NUMBER: 2002:288073 USPATFULL
TITLE: Echinocandin/carbohydrate complexes
INVENTOR(S): Larew, Larry Arnold, Zionsville, IN, UNITED STATES
Milton, Nathaniel, Indianapolis, IN, UNITED STATES
Sabatowski, James Lawrence, Holland, MI, UNITED STATES
Moder, Kenneth Philip, West Lafayette, IN, UNITED STATES

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 2002160942	A1	20021031
APPLICATION INFO.:	US 2001-942458	A1	20010829 (9)

RELATED APPLN. INFO.: Continuation of Ser. No. WO 2000-US5508, filed on 2 Mar 2000, UNKNOWN

	NUMBER	DATE
PRIORITY INFORMATION:	US 1999-122692P	19990303 (60)

DOCUMENT TYPE: Utility
FILE SEGMENT: APPLICATION
LEGAL REPRESENTATIVE: MORRISON & FOERSTER LLP, 755 PAGE MILL RD, PALO ALTO, CA, 94304-1018
NUMBER OF CLAIMS: 27
EXEMPLARY CLAIM: 1
LINE COUNT: 1244

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB A complex of an echinocandin compound with a carbohydrate is described having improved thermal stability and water solubility. A process for making the echinocandin/carbohydrate complex is also described as well as the use of the complex in pharmaceutical formulations and treatments of fungal infections.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L34 ANSWER 5 OF 14 USPATFULL

ACCESSION NUMBER: 2002:102475 USPATFULL

TITLE: Cyclic peptide antifungal agents and process for preparation thereof

INVENTOR(S): Burkhardt, Frederick J., Indianapolis, IN, United States
Debono, Manuel, Indianapolis, IN, United States
Nissen, Jeffrey S., Indianapolis, IN, United States
Turner, Jr., William W., Bloomington, IN, United States

PATENT ASSIGNEE(S): Eli Lilly and Company, Indianapolis, IN, United States (U.S. corporation)

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 6384013	B1	20020507
APPLICATION INFO.:	US 1999-291900		19990414 (9)

RELATED APPLN. INFO.: Continuation-in-part of Ser. No. US 1995-449056, filed on 24 May 1995, now patented, Pat. No. US 5965525 Division of Ser. No. US 1993-32228, filed on 17 Mar 1993, now abandoned
Continuation-in-part of Ser. No. US 1992-992390, filed on 16 Dec 1992, now abandoned
Continuation-in-part of Ser. No. US 1992-854117, filed on 19 Mar 1992, now abandoned

DOCUMENT TYPE: Utility
FILE SEGMENT: GRANTED
PRIMARY EXAMINER: Jones, Dwayne C.
ASSISTANT EXAMINER: Delacroix-Muirheid, C.
LEGAL REPRESENTATIVE: Morrison & Foerster LLP
NUMBER OF CLAIMS: 7
EXEMPLARY CLAIM: 1
NUMBER OF DRAWINGS: 0 Drawing Figure(s); 0 Drawing Page(s)
LINE COUNT: 1079

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB Provided are compounds of the formula (1): ##STR1##

wherein

R' is hydrogen, methyl or NH.sub.2C(O)CH.sub.2--;

R" and R'" are independently methyl or hydrogen;

R and R.sup.y are independently hydroxy or hydrogen;

R.sub.1 is hydroxy, hydrogen, or hydroxysulfonyloxy;

R.sub.7 is hydroxy, hydrogen, hydroxysulfonyloxy or phosphonooxy;

R.sub.2 is a acyl side chain. Also provided are formulations, methods of inhibiting fungal and parasitic activity, and a process for preparing dideoxy (R.dbd.H) forms of the compounds.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L34 ANSWER 6 OF 14 USPATFULL

ACCESSION NUMBER:	2001:215026 USPATFULL
TITLE:	Cyclic peptide antifungal agents
INVENTOR(S):	Jamison, James Andrew, Indianapolis, IN, United States Rodriguez, Michael John, Indianapolis, IN, United States Vasudevan, Venkatraghavan, Indianapolis, IN, United States
PATENT ASSIGNEE(S):	Eli Lilly and Company, United States (U.S. corporation)

	NUMBER	KIND	DATE	
PATENT INFORMATION:	US 6323176	B1	20011127	
APPLICATION INFO.:	US 1999-245572		19990205	(9)

	NUMBER	DATE	
PRIORITY INFORMATION:	US 1998-75882P	19980225	(60)

DOCUMENT TYPE:	Utility
FILE SEGMENT:	GRANTED
PRIMARY EXAMINER:	Davenport, Avis M.
LEGAL REPRESENTATIVE:	Morrison & Foerster LLP
NUMBER OF CLAIMS:	6
EXEMPLARY CLAIM:	1
LINE COUNT:	1053

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB The present invention relates to compounds of formula ##STR1##

where R.sup.5 is a sugar moiety. The compounds are useful in inhibiting fungal and parasitic activity and infections.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L34 ANSWER 7 OF 14 USPATFULL

ACCESSION NUMBER:	2001:199724 USPATFULL
TITLE:	Intranasal cyclic peptide formulations
INVENTOR(S):	Horii, Ikuo, Yokohama-shi, Japan Kobayashi, Kazuko, Kamakura-shi, Japan Shimma, Nobuo, Chigasaki-shi, Japan Yanagawa, Akira, Yokohama-shi, Japan

	NUMBER	KIND	DATE	
PATENT INFORMATION:	US 2001038824	A1	20011108	
APPLICATION INFO.:	US 2001-765846	A1	20010119	(9)

	NUMBER	DATE
PRIORITY INFORMATION:	ET 2000-101057	20000120

DOCUMENT TYPE: Utility
FILE SEGMENT: APPLICATION
LEGAL REPRESENTATIVE: George W. Johnston, Hoffmann-La Roche Inc., 340 Kingsland street, Nutley, NJ, 07110
NUMBER OF CLAIMS: 36
EXEMPLARY CLAIM: 1
NUMBER OF DRAWINGS: 11 Drawing Page(s)
LINE COUNT: 3690
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB The present invention relates to a nasally administrable composition of a physiologically active cyclic peptide and pharmaceutically acceptable salts thereof that is prepared by homogeneously dispersing a physiologically active cyclic peptide such as antifungal cyclic peptides (aerothricins, echinocandin analogs, pneumocandin analogs, and aureobacidines), antibacterial cyclic peptides (e.g. vancomycin, daptomycin), cyclosporin A, lanreotide, vapreotide, vasopressin antagonist (U.S. Pat. No. 5,095,003) and eptifibatide in unique carrier, i.e. a physiologically acceptable powdery or crystalline carrier containing a water insoluble polyvalent metal carrier, or organic carrier having a mean particle size of 20 to 500 .mu.m, in the presence or absence of an absorption enhancer and by homogeneously adsorbing onto the carrier, and its use for therapeutic treatment of disease such as systemic fungal infections by intranasal administration.

The composition can be nasally administered in powder form.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L34 ANSWER 8 OF 14 USPATFULL
ACCESSION NUMBER: 2000:174113 USPATFULL
TITLE: EDTA and other chelators with or without antifungal antimicrobial agents for the prevention and treatment of fungal infections
INVENTOR(S): Raad, Issam, Houston, TX, United States
Sheretz, Robert, Winston-Salem, NC, United States
Hachem, Ray, Houston, TX, United States
PATENT ASSIGNEE(S): Wake Forest University, Winston Salem, NC, United States (U.S. corporation)
Board of Regents, The University of Texas Sysytem, Austin, TX, United States (U.S. corporation)

	NUMBER	KIND	DATE	
PATENT INFORMATION:	US 6165484		20001226	
APPLICATION INFO.:	US 1998-139522		19980825	(9)

	NUMBER	DATE	
PRIORITY INFORMATION:	US 1997-56970P	19970826	(60)

DOCUMENT TYPE: Utility
FILE SEGMENT: Granted
PRIMARY EXAMINER: Weddington, Kevin E.
LEGAL REPRESENTATIVE: Fulbright & Jaworski
NUMBER OF CLAIMS: 10
EXEMPLARY CLAIM: 1

NUMBER OF DRAWINGS: 11 Drawing Figure(s); 11 Drawing Page(s)
LINE COUNT: 1659
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB A pharmaceutical composition comprising at least one antifungal agent and at least one chelator, and a method for administering the pharmaceutical composition to a patient having a fungal infection. Another aspect provides a pharmaceutical composition comprising at least one chelator, at least one antifungal agent and at least one monoclonal antibody, wherein the monoclonal antibody is operatively attached to the chelator, and a method of administering this composition to a patient having a fungal infection.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L34 ANSWER 9 OF 14 USPATFULL
ACCESSION NUMBER: 2000:37897 USPATFULL
TITLE: Cyclic peptide antifungal agents
INVENTOR(S): Udodong, Uko Effiong, Indianapolis, IN, United States
Grutsch, Jr., John Leo, Indianapolis, IN, United States
Hansen, Marvin Martin, Indianapolis, IN, United States
Harkness, Allen Robert, Indianapolis, IN, United States
Verral, II, Daniel Edward, Clinton, IN, United States
PATENT ASSIGNEE(S): Eli Lilly & Co., Indianapolis, IN, United States (U.S. corporation)

	NUMBER	KIND	DATE	
PATENT INFORMATION:	US 6043341		20000328	
APPLICATION INFO.:	US 1998-129062		19980804	(9)

	NUMBER	DATE	
PRIORITY INFORMATION:	US 1997-54538P	19970804	(60)

DOCUMENT TYPE: Utility
FILE SEGMENT: Granted
PRIMARY EXAMINER: Russel, Jeffrey E.
LEGAL REPRESENTATIVE: Morrison & Foerster, LLP
NUMBER OF CLAIMS: 21
EXEMPLARY CLAIM: 5
LINE COUNT: 1953
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB The present invention provides phosphonylating agents and phosphonylation conditions that are compatible with the acid- and base-sensitive compounds and which promote a regioselective and reproducible conversion to a phosphonate compound. Also provided are intermediates that may be used to prepare phosphonate derivatives of cyclic peptides antifungal agent and a process for converting the phosphonates to the desired phosphonic acid prodrugs.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L34 ANSWER 10 OF 14 USPATFULL
ACCESSION NUMBER: 97:66102 USPATFULL
TITLE: Cyclic peptide antifungal agents
INVENTOR(S): Jamison, James A., Indianapolis, IN, United States
Rodriguez, Michael J., Indianapolis, IN, United States
LaGrandeur, Lisa M. H., Tucson, AZ, United States
Turner, William W., Bloomington, IN, United States
Zweifel, Mark J., Indianapolis, IN, United States
PATENT ASSIGNEE(S): Eli Lilly and Company, Indianapolis, IN, United States (U.S. corporation)

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 5652213		19970729
APPLICATION INFO.:	US 1996-613949		19960311 (8)

RELATED APPLN. INFO.: Continuation of Ser. No. US 1995-453052, filed on 26 May 1995
DOCUMENT TYPE: Utility
FILE SEGMENT: Granted
PRIMARY EXAMINER: Schain, Howard E.
LEGAL REPRESENTATIVE: McClain, Janet T., Boone, David E.
NUMBER OF CLAIMS: 65
EXEMPLARY CLAIM: 1
LINE COUNT: 2446
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB Provided are pharmaceutical formulations, and methods of inhibiting fungal and parasitic activity using a compound of formula I: ##STR1## wherein R', R", R.sup.x1, R.sup.x2, R.sup.y1 -R.sup.y4, R.sup.z1, R.sup.z2, a, b, c, d, e, R.sup.0, R.sup.1 and R.sup.2 are defined as in the specification.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L34 ANSWER 11 OF 14 USPATFULL
ACCESSION NUMBER: 97:59170 USPATFULL
TITLE: Cyclic peptide antifungal Agents
INVENTOR(S): Borromeo, Peter S., Fishers, IN, United States
Jamison, James A., Indianapolis, IN, United States
Rodriguez, Michael J., Indianapolis, IN, United States
Turner, William W., Bloomington, IN, United States
Vasudevan, Venkatraghaven, Indianapolis, IN, United States
PATENT ASSIGNEE(S): Eli Lilly and Company, Indianapolis, IN, United States (U.S. corporation)

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 5646111		19970708
APPLICATION INFO.:	US 1996-612208		19960307 (8)

RELATED APPLN. INFO.: Continuation of Ser. No. US 1995-418341, filed on 7 Apr 1995, now abandoned
DOCUMENT TYPE: Utility

FILE SEGMENT: Granted
PRIMARY EXAMINER: Schain, Howard E.
LEGAL REPRESENTATIVE: McClain, Janet T., Boone, David E.
NUMBER OF CLAIMS: 64
EXEMPLARY CLAIM: 1
LINE COUNT: 1964
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB Provided are pharmaceutical formulations, and methods of inhibiting fungal and parasitic activity using a compound of formula I: ##STR1## wherein: R' is hydrogen, methyl or NH.sub.2 C(O)CH.sub.2 --;

R" and R'" are independently methyl or hydrogen;

R.sup.x1, R.sup.x2, R.sup.y1, R.sup.y2, R.sup.y3, and R.sup.y4 are independently hydroxy or hydrogen;

R.sub.0 is a group of the formula ##STR2## R.sub.1 is C.sub.1 -C.sub.6 alkyl, C.sub.1 -C.sub.6 alkoxy, phenyl, p-halo-phenyl, p-nitrophenyl, phenoxy, benzyl, p-halo-benzyl, or p-nitro-benzyl; and

R.sub.2 is an acyl side chain as defined herein.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L34 ANSWER 12 OF 14 USPATFULL
ACCESSION NUMBER: 97:40768 USPATFULL
TITLE: Cyclic peptide antifungal agents
INVENTOR(S): Rodriguez, Michael J., Indianapolis, IN, United States
PATENT ASSIGNEE(S): Eli Lilly and Company, Indianapolis, IN, United States (U.S. corporation)

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 5629289		19970513
APPLICATION INFO.:	US 1995-506790		19950725 (8)

DOCUMENT TYPE: Utility
FILE SEGMENT: Granted
PRIMARY EXAMINER: Tsang, Cecilia
ASSISTANT EXAMINER: Gupta, Anish
LEGAL REPRESENTATIVE: McClain, Janet T., Boone, David E.
NUMBER OF CLAIMS: 24
EXEMPLARY CLAIM: 1
LINE COUNT: 1058
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB Provided are pharmaceutical formulations, and methods of inhibiting fungal and parasitic activity using a compound of formula I: ##STR1## wherein: R.sup.z1 is hydrogen, --CH.sub.2 OH, --CHOHCH.sub.3 or --CHOHCH.sub.2 C(O)NH.sub.2 ;

R.sup.z2 is hydrogen, --CH.sub.2 OH or --CHOHCH.sub.3 ;

R.sup.z3 is hydrogen or methyl;

R.sup.x1 is hydrogen, hydroxy or O--R.sup.x1' ;

R.sup.x1' is C.sub.1 -C.sub.6 alkyl, benzyl, --(CH.sub.2).sub.2 Si(CH.sub.3).sub.3, --CH.sub.2 CH.dbd.CH.sub.2, --CH.sub.2 CHOHCH.sub.2 OH, --(CH.sub.2).sub.a COOH, --(CH.sub.2).sub.b NR.sup.w1 R.sup.w2, --(CH.sub.2).sub.c POR.sup.w3 R.sup.w4 or --[(CH.sub.2).sub.2 O].sub.d --(C.sub.1 -C.sub.6)alkyl;

a, b and c are independently 1, 2, 3, 4, 5 or 6;

R.sup.w1 and R.sup.w2 are independently hydrogen, C.sub.1 -C.sub.6 alkyl, or R.sup.w1 and R.sup.w2 combine to form --CH.sub.2 (CH.sub.2).sub.e CH.sub.2 --;

R.sup.w3 and R.sup.w4 are independently hydroxy, or C.sub.1 -C.sub.6 alkoxy;

d is 1 or 2;

e is 1, 2 or 3;

R.sup.x2, R.sup.y1, R.sup.y2, R.sup.y3 and R.sup.y4 are independently hydroxy or hydrogen;

R.sup.0 is hydroxy, --OP(O)(OH).sub.2 or a group of the formulae: ##STR2## R.sup.1 is C.sub.1 -C.sub.6 alkyl, phenyl, p-halo-phenyl, p-nitrophenyl, benzyl, p-halo-benzyl or p-nitro-benzyl;

R.sup.2 is ##STR3## R.sup.3 is ##STR4## R.sup.3a, R.sup.3b, R.sup.3c and R.sup.3d are independently hydrogen, C.sub.1 -C.sub.12 alkyl, C.sub.2 -C.sub.12 alkynyl, C.sub.1 -C.sub.12 alkoxy, C.sub.1 -C.sub.12 alkylthio, halo, --O--(CH.sub.2).sub.m --[O--(CH.sub.2).sub.n].sub.p --O--(C.sub.1 -C.sub.12 alkyl) or --O--(CH.sub.2).sub.q --X--R.sup.4 ;

m is 2, 3 or 4;

n is 2, 3 or 4;

p is 0 or 1;

q is 2, 3 or 4;

X is pyrrolidino, piperidino or piperazino; and

R.sup.4 is hydrogen, C.sub.1 -C.sub.12 alkyl, C.sub.3 -C.sub.12 cycloalkyl, benzyl or C.sub.3 -C.sub.12 cycloalkylmethyl;

with the proviso that at least one of R.sup.z1 and R.sup.z2 must be hydrogen;

or a pharmaceutically acceptable salt thereof.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L34 ANSWER 13 OF 14 USPATFULL
ACCESSION NUMBER: 96:67980 USPATFULL
TITLE: Antifungal and anti-pneumocystis compounds, compositions containing such compounds, and methods of use

INVENTOR(S): Balkovec, James M., North Plainfield, NJ, United States
Bouffard, Frances A., Scotch Plains, NJ, United States
Black, Regina M., Cranford, NJ, United States
PATENT ASSIGNEE(S): Merck & Co., Inc., Rahway, NJ, United States (U.S. corporation)

	NUMBER	KIND	DATE	
PATENT INFORMATION:	US 5541160		19960730	
APPLICATION INFO.:	US 1994-222157		19940404	(8)

DOCUMENT TYPE: Utility
FILE SEGMENT: Granted
PRIMARY EXAMINER: Gibson, Sharon
ASSISTANT EXAMINER: Scalzo, Catherine S. Kilby
LEGAL REPRESENTATIVE: Korsen, Elliott, Daniel, Mark R.
NUMBER OF CLAIMS: 12
EXEMPLARY CLAIM: 1
LINE COUNT: 1240
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB Compounds represented by the formula I (SEQ ID NO. 1) are disclosed: ##STR1## as well as pharmaceutically acceptable salts and hydrates thereof. R.sup.I represents C.sub.9 to C.sub.19 alkyl, C.sub.9 to C.sub.19 alkenyl, an aryl group which includes phenyl, biphenyl, naphthyl and terphenyl or a C.sub.1 to C.sub.12 alkyl, alkylamino, dialkylamino or alkoxyaryl group.

R.sup.1, R.sup.2 and R.sup.4 independently represent H or --OH.

R.sup.3 represents H, --OH, --O(CH.sub.2).sub.n NR.sup.V R.sup.VI, where R.sup.V and R.sup.VI independently represent H or C.sub.1-4 alkyl, or --O(CH.sub.2).sub.n NR.sup.V R.sup.VI R.sup.VII+ Y.sup.-, wherein R.sup.V and R.sup.VI are as defined above, R.sup.VII represents H or C.sub.1-4 alkyl, n is an integer of from 2-6 inclusive, and Y represents a counterion.

R.sup.5 represents H, --CH.sub.3 or --OH;

R.sup.6 represents H or --CH.sub.3 ;

R.sup.7 represents H, --CH.sub.3, --CH.sub.2 C(.dbd.O)NH.sub.2, --(CH.sub.2).sub.2 NR.sup.V R.sup.VI or --(CH.sub.2).sub.2 NR.sup.V R.sup.VI R.sup.VII+ Y.sup.- with n, R.sup.V, R.sup.VI R.sup.VII and Y as defined above;

and R.sup.8 represents --Cl, --Br, --I, --NO.sub.2, --N.sub.3, --(CH.sub.2).sub.0-4 NH.sub.2, --(CH.sub.2).sub.0-4 NH(C.sub.1-4 alkyl), --(CH.sub.2).sub.0-4 N(C.sub.1-4 alkyl).sub.2, --(CH.sub.2).sub.0-3 CH(.dbd.NOH), --NHC(.dbd.O)(CH.sub.2).sub.1-6 NH.sub.2 or --NHC(.dbd.O)(CH.sub.2).sub.1-6 NHC(.dbd.NH)(CH.sub.2).sub.0-3 H.

Pharmaceutical compositions and methods of use are also disclosed.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L34 ANSWER 14 OF 14 USPATFULL

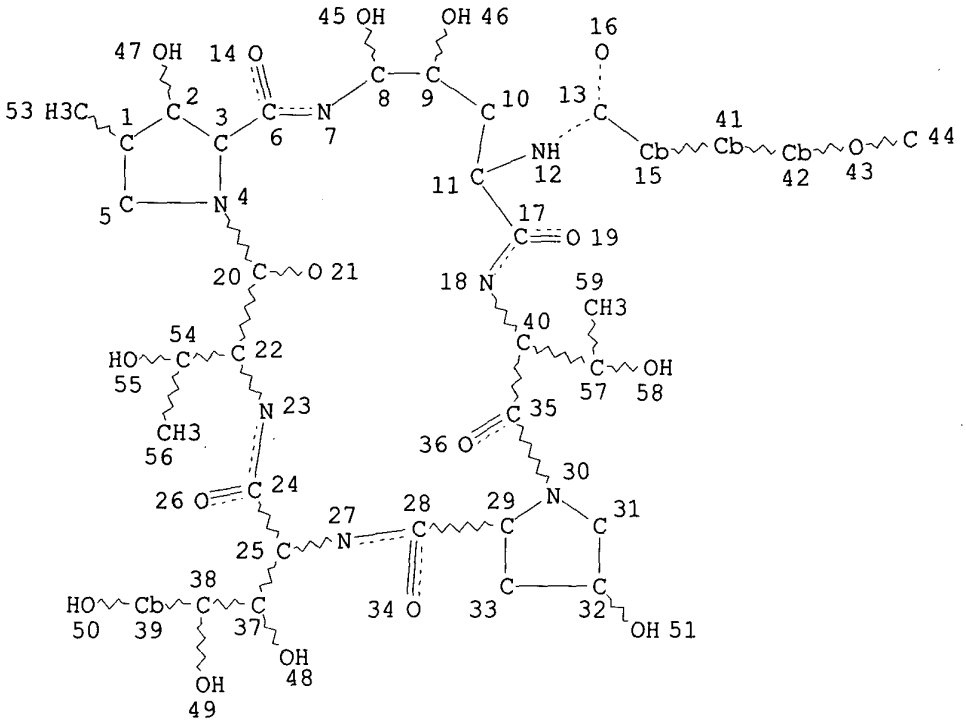
ACCESSION NUMBER: 96:38874 USPATFULL
TITLE: Aza cyclohexapeptide compounds
INVENTOR(S): Balkovec, James M., North Plainfield, NJ, United States
Bouffard, Frances A., Scotch Plains, NJ, United States
Dropinski, James F., Piscataway, NJ, United States
PATENT ASSIGNEE(S): Merck & Co., Inc., Rahway, NJ, United States (U.S. corporation)

	NUMBER	KIND	DATE	
PATENT INFORMATION:	US 5514651		19960507	
APPLICATION INFO.:	US 1994-307978		19940916	(8)

DOCUMENT TYPE: Utility
FILE SEGMENT: Granted
PRIMARY EXAMINER: Chan, Christina Y.
ASSISTANT EXAMINER: Wessendorf, T. D.
LEGAL REPRESENTATIVE: Korsen, Elliott, Daniel, Mark R.
NUMBER OF CLAIMS: 5
EXEMPLARY CLAIM: 1,5
LINE COUNT: 1332
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB The present invention relates to aza cyclohexapeptide compounds of the formula (Seq ID Nos. 1-10) ##STR1## which may be useful as antibiotics, antifungal agents and for the treatment of Pneumocystis carinii infections.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

(FILE 'MARPAT' ENTERED AT 15:05:43 ON 06 JUN 2003)
L35 STR



NODE ATTRIBUTES:
DEFAULT MLEVEL IS ATOM
MLEVEL IS CLASS AT 15 39 41 42
GGCAT IS UNS AT 15
GGCAT IS UNS AT 39
GGCAT IS UNS AT 41
GGCAT IS UNS AT 42
DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:
RING(S) ARE ISOLATED OR EMBEDDED
NUMBER OF NODES IS 58

STEREO ATTRIBUTES: NONE

ATTRIBUTES SPECIFIED AT SEARCH-TIME:
ECLEVEL IS LIM ON ALL NODES
ALL RING(S) ARE ISOLATED

L36 17 SEA FILE=MARPAT SSS FUL L35 (MODIFIED ATTRIBUTES)

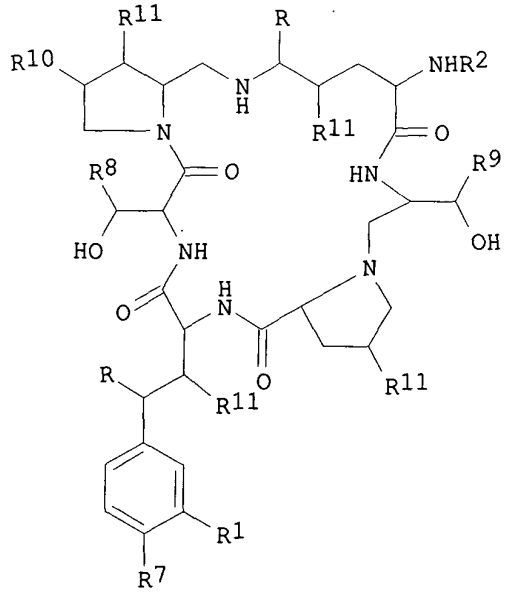
100.0% PROCESSED 100 ITERATIONS 17 ANSWERS
SEARCH TIME: 00.00.02

L36 ANSWER 1 OF 17 MARPAT COPYRIGHT 2003 ACS
ACCESSION NUMBER: 136:341005 MARPAT
TITLE: Preparation of cyclic peptide antifungal agents
INVENTOR(S): Burkhardt, Frederick J.; Debono, Manuel; Nissen,

Jeffrey S.; Turner, William W., Jr.
PATENT ASSIGNEE(S): Eli Lilly and Company, USA
SOURCE: U.S., 33 pp., Cont.-in-part of U.S. 5,965,525.
CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 6384013	B1	20020507	US 1999-291900	19990414
ZA 9301830	A	19940915	ZA 1993-1830	19930315
IL 122315	A1	20020310	IL 1993-122315	19930315
JP 2002226500	A2	20020814	JP 2002-3969	19930318
US 5965525	A	19991012	US 1995-449056	19950524
US 5932543	A	19990803	US 1997-873480	19970612
PRIORITY APPLN. INFO.:			US 1992-854117	19920319
			US 1992-992390	19921216
			US 1993-32228	19930317
			US 1995-449056	19950524
			IL 1993-105048	19930315
			JP 1993-58529	19930318

GI



I

AB Acyl cyclic peptides I (R, R11 = H, OH; R1 = H, OH, OSO3H; R2 = an acyl side chain; R7 = R1, phosphonooxy; R8 = H, Me, H2NCOCH2; R9, R10 = Me, H) were prepd. as fungicides. Thus, I [R = R11 = OH, R1 = H, R2 = p-(pentyoxy)-p-terphenyl, R8 = R9 = R10 = Me, R7 = phosphonooxy] was prepd. in chiral form (echinocandin B deriv.) by

N-acylation and selective O-phosphonylation. Compds. I are esp. active against the infectious fungi Candida albicans and Candida parasilosis and inhibit the growth of Pneumocystis carinii, the causative organism of pneumocystis pneumonia in AIDs sufferers.

IC ICM A61K038-00
NCL 514011000
CC 34-3 (Amino Acids, Peptides, and Proteins)
Section cross-reference(s): 1
ST peptide cyclic prepn fungicide; echinocandin analog prepn fungicide
IT Peptides, preparation
RL: BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(cyclic; prepn. of cyclic peptides as fungicides)
IT Fungicides
(prepn. of cyclic peptides as fungicides)
IT 158935-94-5P 158935-95-6P 158935-96-7P 158935-97-8P
158935-98-9P 158935-99-0P 158936-00-6P 158936-01-7P
158936-02-8P 158936-03-9P 158936-04-0P 158936-05-1P
158936-06-2P 158936-07-3P 158936-08-4P 158936-09-5P
158936-10-8P 158936-11-9P 158936-12-0P 158936-13-1P
158936-14-2P 158936-15-3P 158936-16-4P 158936-17-5P
158936-18-6P 158936-19-7P 158936-20-0P 158936-21-1P
158936-22-2P 158936-23-3P 158936-24-4P 158936-25-5P
158936-26-6P 158936-27-7P 158936-28-8P 158936-29-9P
158936-30-2P 158936-31-3P 158936-32-4P 158936-33-5P
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158936-38-0P 158936-39-1P 158936-40-4P 158936-41-5P
158936-42-6P 158936-43-7P 158936-44-8P 158936-45-9P
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158936-66-4P 158936-67-5P 158936-68-6P 158936-69-7P
158936-70-0P 158936-71-1P 158936-72-2P 158936-73-3P
158936-74-4P 158936-75-5P 158936-76-6P 158936-77-7P
158936-78-8P 158936-79-9P 158936-80-2P 158936-81-3P
158936-82-4P 158936-83-5P 158936-84-6P 158936-85-7P
158936-86-8P 158936-87-9P 158936-88-0P 158936-89-1P
158936-90-4P 158936-91-5P 159000-67-6P 166663-26-9P
166663-28-1P 183211-59-8P 183211-60-1P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of cyclic peptides as fungicides)
IT 107-08-4, 1-Iodopropane 107-82-4 110-53-2, 1-Bromopentane
111-66-0, 1-Octene 536-74-3 540-38-5, 4-Iodophenol 542-69-8,
1-Iodobutane 619-44-3, Methyl 4-iodobenzoate 629-05-0, 1-Octyne
638-45-9, 1-Iodohexane 693-02-7, 1-Hexyne 764-93-2, 1-Decyne
1066-54-2 1647-26-3, 1-Bromo-2-cyclohexylethane 2038-91-7
2346-07-8 2527-99-3, Methyl 5-bromofuran-2-carboxylate
2916-68-9, 2-(Trimethylsilyl)ethanol 3034-86-4 6661-54-7
13295-53-9, Cyclobutylmethyl tosylate 21856-53-1,
Cyclopentylmethyl tosylate 29558-77-8 60834-63-1 62124-28-1
63619-51-2 63619-63-6 63619-64-7 79404-91-4, Cilofungin
79411-15-7 108366-80-9 141430-54-8 158407-15-9 158937-74-7
158937-75-8 158937-76-9 158937-77-0 158937-78-1 158937-79-2

158937-80-5 158937-81-6 158937-82-7 158937-83-8 158937-84-9
158937-85-0
RL: RCT (Reactant); RACT (Reactant or reagent)
(prepn. of cyclic peptides as fungicides)
IT 166663-25-8P 213669-65-9P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation);
RACT (Reactant or reagent)
(prepn. of cyclic peptides as fungicides)
IT 5731-15-7P 25739-23-5P 41424-11-7P 42497-80-3P 52364-71-3P
52709-87-2P 59748-14-0P 59748-15-1P 59748-16-2P 75867-41-3P
82175-72-2P 89752-76-1P 117802-43-4P 117802-44-5P
118788-02-6P 140714-91-6P 144493-15-2P 144540-61-4P
158936-92-6P 158936-93-7P 158936-94-8P 158936-95-9P
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158937-96-3P 158937-97-4P 158937-98-5P 158937-99-6P
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158938-04-6P 158938-05-7P 158938-06-8P 158938-07-9P
158938-08-0P 158938-09-1P 158938-10-4P 158938-11-5P
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158938-16-0P 158938-17-1P 160442-19-3P
RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn. of cyclic peptides as fungicides)
REFERENCE COUNT: 30 THERE ARE 30 CITED REFERENCES AVAILABLE
FOR THIS RECORD. ALL CITATIONS AVAILABLE
IN THE RE FORMAT

L36 ANSWER 2 OF 17 MARPAT COPYRIGHT 2003 ACS
ACCESSION NUMBER: 133:227789 MARPAT
TITLE: Processes for making pharmaceutical oral echinocandin formulations and compositions
INVENTOR(S): Schwier, John Richard; Taylor, Jerry
PATENT ASSIGNEE(S): Eli Lilly and Company, USA
SOURCE: PCT Int. Appl., 40 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000051567	A1	20000908	WO 2000-US5547	20000302
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, GM, HR, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
EP 1156784	A1	20011128	EP 2000-912160	20000302
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
BR 2000008713	A	20011226	BR 2000-8713	20000302
JP 2002538097	T2	20021112	JP 2000-602036	20000302
US 2002151474	A1	20021017	US 2001-942435	20010829
PRIORITY APPLN. INFO.:			US 1999-122693P	19990303
			WO 2000-US5547	20000302

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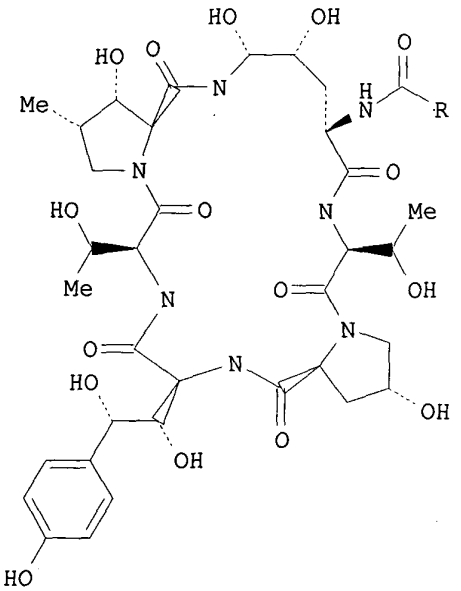

I

AB A fluid bed spray process is described where one or more carbohydrates are incorporated into an echinocandin formulation to provide a significant improvement in thermal stability. The carbohydrate is solubilized with an echinocandin compd. or echinocandin/carbohydrate complex in a solvent(s) to form a pharmaceutical soln. which is sprayed onto the surface of a granular

diluent or carrier. Alternatively, a granulating agent is added to the pharmaceutical soln. which is then sprayed onto the surface of a non-granular diluent or carrier. I was prepd., and a fructose complex with I also prepd.

IC ICM A61K009-16
ICS A61K038-12; A61P031-10

CC 63-6 (Pharmaceuticals)
Section cross-reference(s): 26

ST echinocandin carbohydrate complex prepn pharmaceutical antifungal

IT Drug delivery systems
(oral; prepn. of echinocandin carbohydrate complexes for oral pharmaceuticals)

IT Fungicides
(prepn. of echinocandin carbohydrate complexes for oral pharmaceuticals)

IT Polyoxyalkylenes, biological studies
RL: MOA (Modifier or additive use); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(prepn. of echinocandin carbohydrate complexes for oral pharmaceuticals)

IT Carbohydrates, biological studies
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(prepn. of echinocandin carbohydrate complexes for oral pharmaceuticals)

IT Drug delivery systems
(sachets; prepn. of echinocandin carbohydrate complexes for oral pharmaceuticals)

IT Drug delivery systems
(tablets; prepn. of echinocandin carbohydrate complexes for oral pharmaceuticals)

IT 9003-39-8, Pvp 9004-65-3, Hpmc 9050-31-1, Hydroxypropyl methyl cellulose phthalate 25322-68-3
RL: MOA (Modifier or additive use); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(prepn. of echinocandin carbohydrate complexes for oral pharmaceuticals)

IT 124-63-0, Methanesulfonyl chloride 619-44-3, Methyl 4-iodobenzoate 628-17-1, 1-Iodopentane 29558-77-8, 4-Bromo-4'-hydroxybiphenyl 71849-58-6, Hydroxybenzotriazole
RL: RCT (Reactant); RACT (Reactant or reagent)
(prepn. of echinocandin carbohydrate complexes for oral pharmaceuticals)

IT 54769-22-1P 63619-51-2P, 4-Bromo-4'-pentyloxybiphenyl 158937-25-8P 158937-30-5P 158938-08-0P 220115-71-9P 290826-97-0P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(prepn. of echinocandin carbohydrate complexes for oral pharmaceuticals)

IT 183211-59-8P
RL: RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
(prepn. of echinocandin carbohydrate complexes for oral pharmaceuticals)

IT 57-48-7, Fructose, biological studies
RL: RCT (Reactant); THU (Therapeutic use); BIOL (Biological study); RACT (Reactant or reagent); USES (Uses)

(prepn. of echinocandin carbohydrate complexes for oral pharmaceuticals)

IT 80619-41-6DP, Echinocandin, derivs. 183211-59-8DP, complex with carbohydrates
RL: SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of echinocandin carbohydrate complexes for oral pharmaceuticals)

IT 50-69-1, Ribose 50-70-4, Sorbitol, biological studies 50-81-7, Ascorbic acid, biological studies 50-99-7, Glucose, biological studies 57-50-1, biological studies 58-86-6, Xylose, biological studies 59-23-4, Galactose, biological studies 63-42-3 65-42-9, Lyxose 69-65-8, Mannitol 69-79-4, Maltose 87-79-6, Sorbose 87-89-8, Inositol 87-99-0, Xylitol 99-20-7, Trehalose 115-77-5, biological studies 147-81-9, Arabinose 488-81-3, Adonitol 488-82-4, D-Arabitol 512-69-6, Raffinose 528-50-7, D-Cellobiose 533-50-6 533-67-5, 2-Deoxy-D-ribose 585-88-6, Maltitol 585-99-9, Melibiose 597-12-6, Melezitose 608-66-2, Dulcitol 1109-28-0, Maltotriose 1398-61-4, Chitin 2152-56-9, Arabitol 2438-80-4, Fucose 3458-28-4, Mannose 3615-41-6, Rhamnose 4618-18-2, Lactulose 5328-37-0, L-Arabinose 7643-75-6, L-Arabitol 9004-34-6, Cellulose, biological studies 9005-25-8, Starch, biological studies 13718-94-0, Palatinose
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(prepn. of echinocandin carbohydrate complexes for oral pharmaceuticals)

REFERENCE COUNT: 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L36 ANSWER 3 OF 17 MARPAT COPYRIGHT 2003 ACS
ACCESSION NUMBER: 133:227787 MARPAT
TITLE: Echinocandin pharmaceutical formulations containing micelle-forming surfactants
INVENTOR(S): Milton, Nathaniel; Moder, Kenneth Philip; Sabatowski, James Lawrence; Sweetana, Stephanie Ann
PATENT ASSIGNEE(S): Eli Lilly and Company, USA
SOURCE: PCT Int. Appl., 44 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000051564	A1	20000908	WO 2000-US5546	20000302
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, EE, ES, FI, GB, GE, GH, GM, HR, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
BR 2000009249	A	20011120	BR 2000-9249	20000302

EP 1156782 A1 20011128 EP 2000-910391 20000302
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO
JP 2002538095 T2 20021112 JP 2000-602034 20000302
US 2003054981 A1 20030320 US 2001-942431 20010829
PRIORITY APPLN. INFO.: US 1999-122623P 19990303
WO 2000-US5546 20000302

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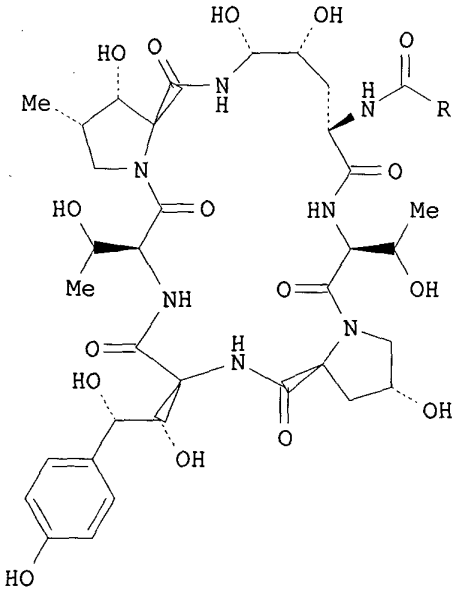

I

AB Pharmaceutical formulations are described comprising an echinocandin compd. or echinocandin/carbohydrate complex and a pharmaceutically acceptable micelle-forming surfactant in a non-toxic aq. solvent such that the solubilization of the echinocandin compd. is optimized and the ability to freeze-dry the soln. is maintained. Both the soln. and freeze-dried formulations have increased stability. A bulking agent, tonicity agent buffer and/or a stabilizing agent may optionally be added to the formulations to further enhance the stability of the formulation. I was prepd. and a freeze-dried prepn. was prepd. contg. I, mannitol and trehalose.

IC ICM A61K009-107
ICS A61K009-19; A61P031-10
CC 63-6 (Pharmaceuticals)
Section cross-reference(s): 26
ST echinocandin pharmaceutical micelle surfactant
IT Micelles
Surfactants
(echinocandin pharmaceutical formulations contg. micelle-forming surfactants)
IT Bile salts
Lecithins

Polyoxyalkylenes, biological studies
RL: MOA (Modifier or additive use); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(echinocandin pharmaceutical formulations contg. micelle-forming surfactants)

IT Drug delivery systems
(freeze-dried; echinocandin pharmaceutical formulations contg. micelle-forming surfactants)

IT 56-14-4, Succinate, biological studies 71-50-1, Acetate, biological studies 126-44-3, Citrate, biological studies 3715-17-1, biological studies 14265-44-2, Phosphate, biological studies
RL: MOA (Modifier or additive use); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(buffer; echinocandin pharmaceutical formulations contg. micelle-forming surfactants)

IT 50-70-4, Sorbitol, biological studies 50-99-7, Dextrose, biological studies 56-40-6, Glycine, biological studies 56-81-5, 1,2,3-Propanetriol, biological studies 56-87-1, L-Lysine, biological studies 57-48-7, Fructose, biological studies 57-50-1, biological studies 57-55-6, 1,2-Propanediol, biological studies 63-42-3 64-17-5, Ethanol, biological studies 69-65-8, D-Mannitol 71-00-1, Histidine, biological studies 99-20-7, Trehalose 7647-14-5, Sodium chloride, biological studies 7732-18-5, Water, biological studies 7757-82-6, Sodium sulfate, biological studies 9004-99-3, Polyoxyethylene stearate 25322-68-3 26266-58-0, Sorbitan trioleate
RL: MOA (Modifier or additive use); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(echinocandin pharmaceutical formulations contg. micelle-forming surfactants)

IT 124-63-0, Methanesulfonyl chloride 628-17-1, 1-Iodopentane 29558-77-8, 4-Bromo-4'-hydroxybiphenyl 71849-58-6, Hydroxybenzotriazole
RL: RCT (Reactant); RACT (Reactant or reagent)
(echinocandin pharmaceutical formulations contg. micelle-forming surfactants)

IT 54769-22-1P 63619-51-2P, 4-Bromo-4'-pentyloxybiphenyl 158937-25-8P 158937-30-5P 158938-08-0P 220115-71-9P 290826-97-0P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(echinocandin pharmaceutical formulations contg. micelle-forming surfactants)

IT 183211-59-8P
RL: SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(echinocandin pharmaceutical formulations contg. micelle-forming surfactants)

IT 80619-41-6, Echinocandin
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(echinocandin pharmaceutical formulations contg. micelle-forming surfactants)

REFERENCE COUNT: 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L36 ANSWER 4 OF 17 MARPAT COPYRIGHT 2003 ACS

ACCESSION NUMBER: 133:222965 MARPAT
TITLE: Preparation of echinocandin/carbohydrate complexes as fungicides
INVENTOR(S): Larew, Larry Arnold; Milton, Nathaniel; Sabatowski, James Lawrence; Moder, Kenneth Philip
PATENT ASSIGNEE(S): Eli Lilly and Co., USA
SOURCE: PCT Int. Appl., 35 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000052037	A1	20000908	WO 2000-US5508	20000302
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, GM, HR, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
EP 1157030	A1	20011128	EP 2000-917703	20000302
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
BR 2000008712	A	20011226	BR 2000-8712	20000302
JP 2002539090	T2	20021119	JP 2000-602261	20000302
US 2002160942	A1	20021031	US 2001-942458	20010829
PRIORITY APPLN. INFO.:			US 1999-122692P	19990303
			WO 2000-US5508	20000302

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* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

AB A complex of an echinocandin compd. with a carbohydrates I (R = alkyl, alkenyl, alkynyl, heteroaryl; R1-R3,R6,R7,R10 = independently H, OH; R4 = H, Me, CH2CONH2; R5, R11 = independently Me, H; R8 = OH, OSO3H, OPO3H2, substituted phosphate; R9 = H, OH, OSO3H) were prepd. as fungicides and having improved thermal stability and water soly. Thus, I (R = Z, R1-R3, R6-R8, R10 = OH, R3 = R5 = R11 = Me; R9 = H) was prepd. and complexed with fructose and tested in vitro as antifungal agent.

IC ICM C07K007-56
ICS A61K047-48
CC 33-2 (Carbohydrates)
Section cross-reference(s): 1, 27
ST echinocandin monosaccharide complex prepn fungicide thermal stability
IT Fungicides
Thermal stability
(prepn. of echinocandin/monosaccharide complexes as fungicides)

IT Monosaccharides
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of echinocandin/monosaccharide complexes as fungicides)

IT 291295-10-8P 291295-11-9P 291295-12-0P 291295-13-1P
291295-14-2P 291295-15-3P 291295-16-4P 291295-17-5P
291295-18-6P 291295-19-7P 291295-20-0P 291295-21-1P
291295-22-2P 291295-23-3P 291295-24-4P 291295-25-5P
291295-26-6P 291295-27-7P 291295-28-8P 291295-29-9P
291295-30-2P 291295-31-3P 291295-32-4P 291295-33-5P
291295-34-6P 291295-35-7P 291295-36-8P 291295-37-9P
291295-38-0P 291295-39-1P 291295-40-4P 291295-41-5P
291295-42-6P 291295-43-7P 291295-44-8P 291295-45-9P
291295-46-0P 291295-47-1P 291295-48-2P 291295-49-3P
291295-50-6P 291295-51-7P 291295-52-8P 291295-53-9P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of echinocandin/monosaccharide complexes as fungicides)

IT 628-17-1, 1-Iodopentane 29558-77-8, 4-Bromo-4'-hydroxybiphenyl
80029-43-2
RL: RCT (Reactant); RACT (Reactant or reagent)
(prepn. of echinocandin/monosaccharide complexes as fungicides)

IT 54769-22-1P 63619-51-2P 158937-25-8P 158937-30-5P
158938-08-0P 166663-25-8P 220115-71-9P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(prepn. of echinocandin/monosaccharide complexes as fungicides)

REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L36 ANSWER 5 OF 17 MARPAT COPYRIGHT 2003 ACS
ACCESSION NUMBER: 132:308664 MARPAT
TITLE: Photochemical process for conversion of the 1,2-diol moiety of an echinocandin compound to the 1-deoxy-2-keto analog
INVENTOR(S): Hitchcock, Stephen Andrew; Gregory, George Stuart
PATENT ASSIGNEE(S): Eli Lilly and Company, USA
SOURCE: PCT Int. Appl., 28 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000024694	A1	20000504	WO 1999-US25301	19991027

W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ,

VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG
PRIORITY APPLN. INFO.: US 1998-105936P 19981028
OTHER SOURCE(S): CASREACT 132:308664
AB A method for converting an epoxy or hydroxy moiety to a 1-deoxy-2-keto moiety is described which includes: (1) reacting a compd. having an epoxy or hydroxy moiety with a thiophenol and (2) irradiating the 1-phenylthio-2-hydroxy moiety with UV or near-UV radiation to convert the 1-phenylsulfide-2-hydroxy moiety to a 1-deoxy-2-keto moiety. The process was used to modify the cyclic peptide ring system of an echinocandin-type compd. contg. a 1,2-diol moiety to produce new keto analogs.
IC ICM C07B041-06
ICS C07K007-56
CC 34-3 (Amino Acids, Peptides, and Proteins)
ST echinocandin diol conversion deoxy keto analog; keto analog echinocandin prepn
IT Peptides, preparation
RL: SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(cyclic; photochem. process for conversion of diol moiety of an echinocandin compd. to 1-deoxy-2-keto analog)
IT 266317-26-4P
RL: IMF (Industrial manufacture); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
(photochem. process for conversion of diol moiety of an echinocandin compd. to 1-deoxy-2-keto analog)
IT 266317-27-5P 266317-28-6P
RL: IMF (Industrial manufacture); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(photochem. process for conversion of diol moiety of an echinocandin compd. to 1-deoxy-2-keto analog)
IT 119-26-6, 2,4-Dinitrophenylhydrazine 1099-45-2, Ethyl triphenylphosphoranylideneacetate 37972-89-7, Benzenethiol, 2-iodo- 166663-25-8
RL: RCT (Reactant); RACT (Reactant or reagent)
(photochem. process for conversion of diol moiety of an echinocandin compd. to 1-deoxy-2-keto analog)
IT 266317-25-3P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(photochem. process for conversion of diol moiety of an echinocandin compd. to 1-deoxy-2-keto analog)
REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L36 ANSWER 6 OF 17 MARPAT COPYRIGHT 2003 ACS
ACCESSION NUMBER: 132:208137 MARPAT
TITLE: Reversible boronate complexes of 1,2-cis-diol cyclic peptides
INVENTOR(S): Moser, Brian Allen; Baker, Jeffrey Clayton
PATENT ASSIGNEE(S): Eli Lilly and Company, USA
SOURCE: PCT Int. Appl., 35 pp.

CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000012540	A1	20000309	WO 1999-US19066	19990818
W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SL, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
CA 2340647	AA	20000309	CA 1999-2340647	19990818
AU 9956834	A1	20000321	AU 1999-56834	19990818
EP 1107982	A1	20010620	EP 1999-943807	19990818
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
PRIORITY APPLN. INFO.:			US 1998-98267P	19980828
			WO 1999-US19066	19990818

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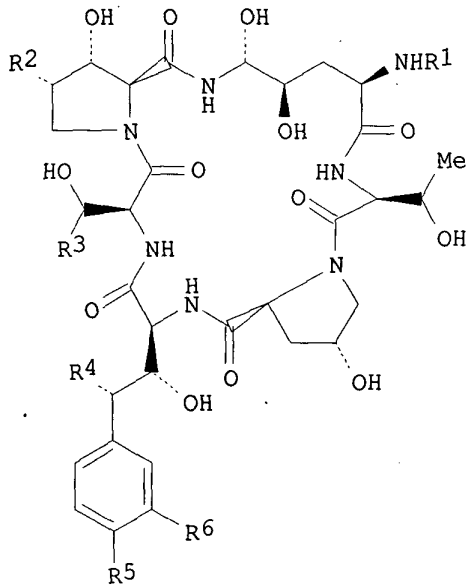

I

AB Reversible borate or boronate complexes of 1,2-cis-diol cyclic peptides are useful for purifn., isolation, stabilization and/or water solubilization of their resp. parent 1,2-cis-diol cyclic

peptides I (R1 = H, acyl; R2 = H, Me; R3 = H, Me, CH2CONH2, CH2CH2NH2; R4 = H, OH; R5 = OH, OPO3H2, OSO3H; R6 = H, OSO3H). The method is particularly useful for forming boronate adducts of hydrophobic echinocandin compds. to increase their water soly. Thus, the soly. of I (R1 = p-pentyloxy-p-terphenylcarbonyl; R2, R3 = Me; R4, R6 = H; R5 = OH) was increased in the presence of m-aminophenylboronic acid (concn. 23.76 mg/mL in supernatant or 94% of the original suspension, vs. 2.27 mg/mL in ammonium bicarbonate control supernatant).

IC ICM C07K007-56
ICS A61K038-12

CC 34-3 (Amino Acids, Peptides, and Proteins)
Section cross-reference(s): 29

ST echinocandin cyclic peptide solubilization boronate complex

IT Peptides, reactions
RL: RCT (Reactant); RACT (Reactant or reagent)
(cyclic; reversible boronate complexes of cis-diol cyclic peptides)

IT 98-80-6, Phenylboronic acid 1765-93-1, p-Fluorophenylboronic acid 4151-80-8 4347-33-5 4426-47-5, Butylboronic acid 4433-63-0, Ethylboronic acid 5467-74-3, p-Bromophenylboronic acid 5720-05-8, p-Methylphenylboronic acid 5720-07-0, p-Methoxyphenylboronic acid 6165-68-0, 2-Thiopheneboronic acid 6165-69-1, 3-Thiopheneboronic acid 13922-41-3, 1-Naphthylboronic acid 14047-29-1, p-Carboxyphenylboronic acid 16419-60-6, o-Methylphenylboronic acid 17745-45-8, Propylboronic acid 24067-17-2, p-Nitrophenylboronic acid 30418-59-8, m-Aminophenylboronic acid 40138-16-7, o-Formylphenylboronic acid 87199-16-4, m-Formylphenylboronic acid 98437-23-1, Benzo[b]thiophene-2-boronic acid 98437-24-2 103681-98-7 128796-39-4 144104-59-6 162607-18-3 206551-43-1 260368-77-2 260369-10-6
RL: RCT (Reactant); RACT (Reactant or reagent)
(reversible boronate complexes of cis-diol cyclic peptides)

REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L36 ANSWER 7 OF 17 MARPAT COPYRIGHT 2003 ACS
ACCESSION NUMBER: 132:194661 MARPAT
TITLE: Preparation of ring modified cyclic peptide analogs as antifungal agents
INVENTOR(S): Borromeo, Peter Stanley; Cohen, Jeffrey Daniel; Gregory, George Stuart; Henle, Stacy Kay; Hitchcock, Stephen Andrew; Jungheim, Louis Nickolaus; Mayhugh, Daniel Ray; Shepherd, Timothy Alan; Turner, William Wilson, Jr.
PATENT ASSIGNEE(S): Eli Lilly and Company, USA
SOURCE: PCT Int. Appl., 108 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM.. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000011023	A2	20000302	WO 1999-US18908	19990818

WO 2000011023 A3 20000615
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, GM, HR, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, SD, SL, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG
CA 2340676 AA 20000302 CA 1999-2340676 19990818
AU 9955726 A1 20000314 AU 1999-55726 19990818
EP 1107981 A2 20010620 EP 1999-942321 19990818
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO
JP 2002528388 T2 20020903 JP 2000-566295 19990818
PRIORITY APPLN. INFO.: US 1998-97228P 19980820
WO 1999-US18908 19990818

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* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

AB A method is provided for modifying the cyclic peptide ring system of echinocandin-type compds. to produce new analogs, e.g., I (R = alkyl, alkenyl, alkynyl, aryl, heteroaryl; R1, R4 = H, OH; R2 = H, Me; R3 = H, Me, CH2CONH2, CH2, CH2NH2; R5 = OH, OPO3H2, OSO3H; R6 = H, OSO3H), having antifungal activity. The process comprises opening the cyclic peptide ring, cleaving the terminal ornithine unit, inserting at least one new amino acid or other synthetic unit and closing the ring to produce a new cyclic peptide ring structure. Thus, cyclic peptide II [R = p-(pentyloxy)-p-terphenyl] was prepd. and showed min. inhibitory concns. 0.005-0.156 .mu.g/mL against four fungi.

IC ICM C07K007-50
ICS A61K038-12
CC 34-3 (Amino Acids, Peptides, and Proteins)
Section cross-reference(s): 10
ST cyclic peptide prepn fungicide

IT Peptides, preparation
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(cyclic; prepn. of ring modified cyclic peptide analogs as antifungal agents)

IT Emulsifying agents
Flavoring materials
Fungicides
Lubricants
Perfumes
Preservatives
Stabilizing agents
Sweetening agents
Wetting agents
(prepn. of ring modified cyclic peptide analogs as antifungal

agents)

IT 259824-88-9P 259825-07-5P 259825-57-5P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
(prepn. of ring modified cyclic peptide analogs as antifungal agents)

IT 259824-75-4P 259824-76-5P 259824-77-6P 259824-78-7P
259824-79-8P 259824-89-0P 259824-91-4P 259824-92-5P
259824-93-6P 259824-94-7P 259824-95-8P 259824-96-9P
259824-97-0P 259825-08-6P 259825-17-7P 259825-30-4P
259825-36-0P 259825-41-7P 259825-42-8P 259825-43-9P
259825-44-0P 259825-45-1P 259825-46-2P 259825-47-3P
259825-48-4P 259825-49-5P 259825-58-6P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of ring modified cyclic peptide analogs as antifungal agents)

IT 50-00-0, Formaldehyde, reactions 75-07-0, Acetaldehyde, reactions 103-72-0, Phenyl isothiocyanate 123-38-6, Propionaldehyde, reactions 672-15-1, L-Homoserine 2389-45-9 2480-93-5 16937-92-1 25508-20-7 56926-94-4 65621-26-3 65710-57-8 68642-94-4 79404-91-4, Cilofungin 118554-00-0 252049-08-4
RL: RCT (Reactant); RACT (Reactant or reagent)
(prepn. of ring modified cyclic peptide analogs as antifungal agents)

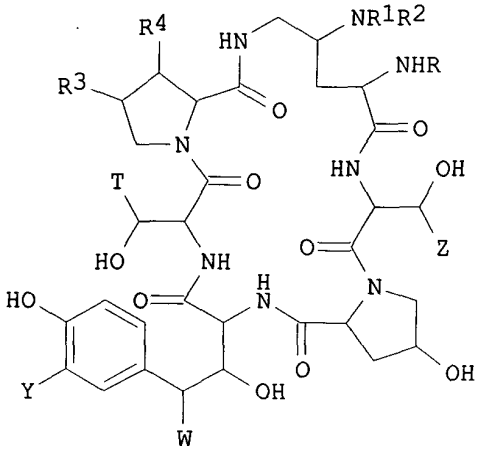
IT 16748-79-1P 30925-18-9P 62234-36-0P 62234-37-1P 76387-70-7P
85003-76-5P 259824-65-2P 259824-67-4P 259824-68-5P
259824-69-6P 259824-70-9P 259824-72-1P 259824-73-2P
259824-74-3P 259824-80-1P 259824-81-2P 259824-82-3P
259824-83-4P 259824-84-5P 259824-85-6P 259824-86-7P
259824-87-8P 259824-98-1P 259824-99-2P 259825-00-8P
259825-01-9P 259825-02-0P 259825-03-1P 259825-04-2P
259825-05-3P 259825-06-4P 259825-09-7P 259825-10-0P
259825-11-1P 259825-12-2P 259825-14-4P 259825-16-6P
259825-20-2P 259825-22-4P 259825-24-6P 259825-25-7P
259825-27-9P 259825-29-1P 259825-31-5P 259825-32-6P
259825-33-7P 259825-34-8P 259825-35-9P 259825-37-1P
259825-38-2P 259825-39-3P 259825-40-6P 259825-50-8P
259825-51-9P 259825-52-0P 259825-53-1P 259825-54-2P
259825-55-3P 259825-56-4P 259825-59-7P 259825-60-0P
259825-61-1P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(prepn. of ring modified cyclic peptide analogs as antifungal agents)

L36 ANSWER 8 OF 17 MARPAT COPYRIGHT 2003 ACS
ACCESSION NUMBER: 131:45105 MARPAT
TITLE: Preparation of Echinocandin B derivatives as antifungal agents
INVENTOR(S): Courtin, Olivier; Fauveau, Patrick; Markus, Astrid; Melon Manguer, Dominique; Michel, Jean-Marc; Schio, Laurent
PATENT ASSIGNEE(S): Hoechst Marion Roussel, Fr.

SOURCE: PCT Int. Appl., 46 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: French
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9929716	A1	19990617	WO 1998-FR2671	19981209
W: AL, AU, BA, BB, BG, BR, CA, CN, CU, CZ, EE, GD, GE, HR, HU, ID, IL, IN, IS, JP, KP, KR, LC, LK, LR, LT, LV, MG, MK, MN, MX, NO, NZ, PL, RO, SG, SI, SK, SL, TR, TT, UA, US, UZ, VN, YU, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
FR 2772028	A1	19990611	FR 1997-15628	19971210
FR 2772028	B1	20000204		
FR 2784993	A1	20000428	FR 1998-13361	19981026
FR 2784993	B1	20021031		
ZA 9811158	A	19991207	ZA 1998-11158	19981207
CA 2311295	AA	19990617	CA 1998-2311295	19981209
AU 9915659	A1	19990628	AU 1999-15659	19981209
AU 755033	B2	20021128		
EP 1036090	A1	20000920	EP 1998-959935	19981209
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, PT, IE, SI, LT, LV, FI, RO				
BR 9813531	A	20001010	BR 1998-13531	19981209
EE 200000336	A	20010815	EE 2000-20000033619981209	
JP 2001525421	T2	20011211	JP 2000-524307	19981209
NZ 504614	A	20021220	NZ 1998-504614	19981209
TW 446541	B	20010721	TW 1998-87121185	19990122
BG 104494	A	20010131	BG 2000-104494	20000531
NO 2000002959	A	20000809	NO 2000-2959	20000609
PRIORITY APPLN. INFO.:			FR 1997-15628	19971210
			FR 1998-13361	19981026
			WO 1998-FR2671	19981209

GI



I

AB The title compds. I (R1, R2 = H, OH, (substituted) alkyl, NR1 forms with the carbon bearing NR1R2 a double bond and R2 = MP; M = O, NH, alkylamino; P = H, (substituted) alkyl; R3 = H, OH, CH3; R4 = H, OH; R = linear or branched chain up to 30 carbon atoms optionally substituted with heteroatoms, aryls or heterocycles; T = H, CH3, CH2CONH2, CH2C.tplbond.N, (CH2)2NH2; Y = H, OH, halogen; W = H, OH; Z = H, CH3) were prepd. as antifungal agents (no data given). For example, 1-[(4R,5R)-4,5-dihydroxy-N2-(12-methyltetradecanoyl)-L-ornithine]-4-[4-(4-hydroxyphenyl)-L-threonine]-5-L-serine-echinocandin B was treated with trimethylsilyl iodide and sodium thiosulfate in succession to give the intermediate 1-[N2-(12-methyltetradecanoyl)-4-oxo-L-ornithine]-4-[4-(4-hydroxyphenyl)-L-threonine]-5-L-serine-echinocandin B in 62% yield. This intermediate, when treated with 2-(dimethylamino)ethylamine, gave the final product I [NR1R2 = NHCH2CH2NMe2, R = CO(CH2)10CH(CH3)CH2CH3, Z = CH3, W = Y = T = H, R3 = CH3, R4 = OH] as a mixt. of isomers, which were, then, sepd. via HPLC.

IC ICM C07K007-56
ICS A61K038-12

CC 34-3 (Amino Acids, Peptides, and Proteins)
Section cross-reference(s): 1

ST echinocandin B deriv prepn antifungal agent

IT Fungicides
(prepn. of echinocandin derivs. as antifungal agents)

IT 227472-27-7P 227472-67-5P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); RCT (Reactant); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent)
(prepn. of echinocandin derivs. as antifungal agents)

IT 227472-29-9P 227472-31-3P 227472-33-5P 227472-34-6P
227472-35-7P 227472-37-9P 227472-38-0P 227472-39-1P
227472-40-4P 227472-41-5P 227472-42-6P 227472-43-7P
227472-45-9P 227472-47-1P 227472-48-2P 227472-49-3P
227472-50-6P 227472-51-7P 227472-62-0P 227472-63-1P
227472-64-2P 227472-66-4P 227472-68-6P 227472-70-0P
227472-72-2P 227472-73-3P 227472-74-4P

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(prepn. of echinocandin derivs. as antifungal agents)

IT 107-15-3, 1,2-Ethanediamine, reactions 108-00-9, 2-(Dimethylamino)ethylamine 109-76-2, 1,3-Diaminopropane 1937-19-5 3279-95-6 55959-84-7 59748-18-4 65920-18-5 227472-53-9 227472-57-3 227614-36-0
RL: RCT (Reactant); RACT (Reactant or reagent)
(prepn. of echinocandin derivs. as antifungal agents)

IT 138626-63-8P, Deoxymulundocandin 160430-95-5P 227472-52-8P 227472-54-0P 227472-55-1P 227472-56-2P 227472-58-4P 227472-59-5P 227472-60-8P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(prepn. of echinocandin derivs. as antifungal agents)

REFERENCE COUNT: 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L36 ANSWER 9 OF 17 MARPAT COPYRIGHT 2003 ACS
ACCESSION NUMBER: 130:139659 MARPAT
TITLE: Phosphonylation agents for synthesis of cyclic peptide antifungal agents
INVENTOR(S): Grutsch, John Leo, Jr.; Hansen, Marvin Martin; Harkness, Allen Robert; Udodong, Uko Effiong; Verral, Daniel Edward, II
PATENT ASSIGNEE(S): Eli Lilly and Company, USA
SOURCE: PCT Int. Appl., 82 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9906062	A1	19990211	WO 1998-US16195	19980803
W: AL, AM, AU, AZ, BA, BB, BG, BR, BY, CA, CN, CU, CZ, EE, GE, GH, GM, HR, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, RO, RU, SD, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
CA 2301184	AA	19990211	CA 1998-2301184	19980803
AU 9886877	A1	19990222	AU 1998-86877	19980803
EP 906915	A1	19990407	EP 1998-306195	19980804
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
US 6043341	A	20000328	US 1998-129062	19980804
PRIORITY APPLN. INFO.:			US 1997-54538P	19970804
			WO 1998-US16195	19980803

AB Phosphonylation agents [R1CH2OPR(O)]2O [R = alkyl, Ph, benzyl; R1 = (un)substituted Ph, naphthyl, cyclohexyl] were prepd. for use in the synthesis of phosphonate derivs. of cyclic peptides antifungal agents. Thus, bis(4-bromobenzyl) dimethylpyrophosphonate was prepd. as a syn/anti mixt. and applied to the phosphonylation of the phenol

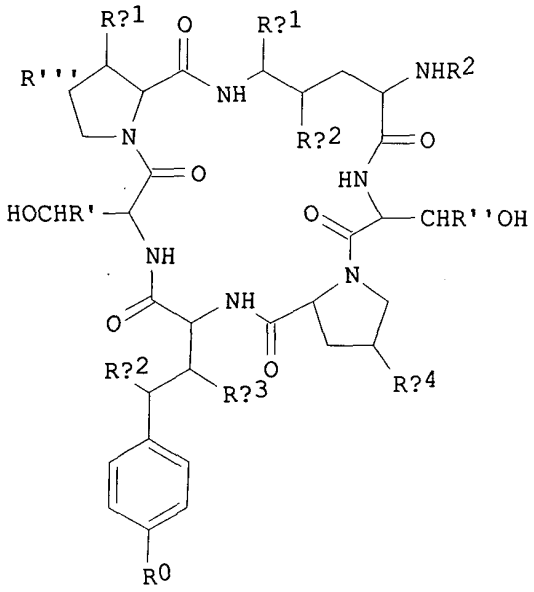
residue of an echinocandin B-related cyclic peptide.
IC ICM A61K038-12
ICS C07F009-40; C07K001-113; C07K007-56
CC 34-3 (Amino Acids, Peptides, and Proteins)
Section cross-reference(s): 10, 29, 33
ST phosponylation agent prepn cyclic peptide antifungal agent
IT Peptides, preparation
RL: SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(cyclic; phosphonylation agents for synthesis of cyclic peptide antifungal agents)
IT Fungicides
Phosphonylation
(phosphonylation agents for synthesis of cyclic peptide antifungal agents)
IT 97-30-3, Methyl .alpha.-D-glucopyranoside 582-52-5, Diacetone-D-glucose 617-04-9, Methyl .alpha.-D-mannopyranoside 619-44-3, Methyl 4-iodobenzoate 628-17-1, 1-Iodopentane 676-97-1, Methylphosphonic dichloride 873-75-6, 4-Bromobenzyl alcohol 1125-88-8, Benzaldehyde dimethyl acetal 5419-55-6, Triisopropyl borate 29558-77-8, 4-Bromo-4'-hydroxybiphenyl 79411-15-7
RL: RCT (Reactant); RACT (Reactant or reagent)
(phosphonylation agents for synthesis of cyclic peptide antifungal agents)
IT 19236-58-9P 54769-22-1P 57701-27-6P 63619-51-2P 74247-81-7P 78738-75-7P 101523-04-0P 158937-25-8P 158937-30-5P 158938-08-0P 166663-25-8P 179118-65-1P 220115-63-9P 220115-64-0P 220115-65-1P 220115-66-2P 220115-67-3P 220115-69-5P 220115-70-8P 220115-71-9P 220115-73-1P 220115-74-2P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(phosphonylation agents for synthesis of cyclic peptide antifungal agents)
IT 19488-48-3P 76333-82-9P 131089-35-5P 162284-50-6P 220115-68-4P 220115-72-0P 220115-75-3P 220115-76-4P 220115-77-5P 220115-78-6P 220115-79-7P 220115-80-0P 220115-82-2P 220115-83-3P 220115-84-4P
RL: SPN (Synthetic preparation); PREP (Preparation)
(phosphonylation agents for synthesis of cyclic peptide antifungal agents)
IT 183211-75-8P
RL: SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(phosphonylation agents for synthesis of cyclic peptide antifungal agents)
REFERENCE COUNT: 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L36 ANSWER 10 OF 17 MARPAT COPYRIGHT 2003 ACS
ACCESSION NUMBER: 128:48495 MARPAT
TITLE: preparation of cyclic peptides as antifungal agents
INVENTOR(S): Henle, Stacy Kay; Turner, William Wilson
PATENT ASSIGNEE(S): Eli Lilly and Co., USA
SOURCE: U.S., 26 pp.

CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 5693611	A	19971202	US 1997-785207	19970117

PRIORITY APPLN. INFO.: US 1997-785207 19970117
GI



I

AB Cyclic peptides I [R' = H, Me, H2NCH2CH2, H2NCOCH2; R'', R''' = H, Me; Rx1 = H, NHR, OR (R = alkyl, benzyl, allyl, etc.); Rx2, Ry1, Ry2, Ry3, Ry4 = H, OH; R0 = OH, OP(O)(OH)2, OP(O)R1OH, OP(O)(OR1)OH (R1 = alkyl, Ph, benzyl, p-halo- or p-nitrophenyl or -benzyl), R2 = CO-A-X-B-Y-C-R3 (A, B, C = benzene, pyridine, pyridazine, pyrimidine, pyrazine, furan or thiophene ring; X, Y, = bond or C.tplbond.C; R3 = alkyl, alkoxy)] or their pharmaceutically acceptable salts were prepd. as antifungal agents. Thus, I [R', R'', R''' = Me; Rx1, Rx2, Ry1, Ry2, Ry3, Ry4, R0 = OH, R2 = [6-[6-[4-(pentyloxy)phenyl]-3-pyridyl]-3-pyridyl]carbonyl] was prepd. tested against C. albicans (min. inhibitory concn. = 0.78 .mu.g/mL).

IC ICM A61K038-00
ICS C07C233-00
NCL 514009000
CC 34-3 (Amino Acids, Peptides, and Proteins)
Section cross-reference(s): 10, 63
ST cyclic peptide prepn antifungal
IT Peptides, preparation

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(cyclic; prepn. of cyclic peptides as antifungal agents)

IT Fungicides
(prepn. of cyclic peptides as antifungal agents)

IT 194482-18-3P 194482-19-4P 194482-20-7P 194482-21-8P
194482-22-9P 194482-23-0P 194482-24-1P 194482-25-2P
194482-26-3P 194482-27-4P 194482-28-5P 194482-29-6P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of cyclic peptides as antifungal agents)

IT 57-13-6, Urea, reactions 106-41-2, 4-Bromophenol 109-94-4, Ethyl formate 110-53-2, 1-Bromopentane 111-70-6, 1-Heptanol 619-44-3 624-28-2, 2,5-Dibromopyridine 628-17-1, 1-Iodopentane 661-69-8, Hexamethylditin 763-69-9 2592-95-2, 1-Hydroxybenzotriazole 5419-55-6, Triisopropyl borate 5751-82-6 13466-38-1, 2-Hydroxy-5-bromopyridine 19812-93-2, 4-Cyano-4'-hydroxybiphenyl 51350-23-3 79411-15-7, Antibiotic A-30912A nucleus
RL: RCT (Reactant); RACT (Reactant or reagent)
(prepn. of cyclic peptides as antifungal agents)

IT 25307-87-3P 30752-18-2P 32779-36-5P 33458-27-4P 54769-22-1P
63619-51-2P 65488-27-9P 73781-91-6P 89793-12-4P 91978-81-3P
123732-04-7P 136370-19-9P 146449-90-3P 158937-25-8P
194481-40-8P 194481-41-9P 194481-43-1P 194481-45-3P
194481-47-5P 194481-49-7P 194481-53-3P 194481-55-5P
194481-59-9P 194481-61-3P 194481-68-0P 194481-74-8P
194481-76-0P 194481-78-2P 194481-80-6P 194481-82-8P
194481-84-0P 194481-86-2P 194481-88-4P 194481-90-8P
194481-91-9P 194481-92-0P 194481-93-1P 194481-94-2P
194481-95-3P 194481-96-4P 194481-97-5P 194481-98-6P
194481-99-7P 194482-00-3P 194482-01-4P 194482-02-5P
194482-03-6P 194482-04-7P 194482-05-8P 194482-06-9P
194482-07-0P 194482-08-1P 194482-09-2P 194482-10-5P
194482-11-6P 194482-12-7P 194482-13-8P 194482-14-9P
194482-15-0P 194482-16-1P 194482-17-2P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(prepn. of cyclic peptides as antifungal agents)

IT 2527-99-3P 40501-41-5P 185317-24-2P
RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn. of cyclic peptides as antifungal agents)

L36 ANSWER 11 OF 17 MARPAT COPYRIGHT 2003 ACS
ACCESSION NUMBER: 127:205892 MARPAT
TITLE: Semisynthesis of cyclic peptide antifungal and antiparasitic agents
INVENTOR(S): Henle, Stacy K.; Turner, William W., Jr.
PATENT ASSIGNEE(S): Eli Lilly and Co., USA
SOURCE: PCT Int. Appl., 68 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9727864	A1	19970807	WO 1997-US1607	19970129
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, HU, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, TJ, TM, TR, TT, UA, UG, UZ, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: KE, LS, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
CA 2244238	AA	19970807	CA 1997-2244238	19970129
AU 9718517	A1	19970822	AU 1997-18517	19970129
EP 881907	A1	19981209	EP 1997-904148	19970129
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, NL, SE, PT, IE, FI				
JP 2001503015	T2	20010306	JP 1997-527861	19970129
PRIORITY APPLN. INFO.:			US 1996-10946P	19960201
			GB 1996-3151	19960215
			WO 1997-US1607	19970129

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* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

AB Cyclic peptide compds. I [R1 = H, Me, CH2CH2NH2, CH2CONH2; R2, R3 = independently H, Me; R4 = H, OH, NHR, OR; R = C1-6 alkyl, CH2Ph, (CH2)2SiMe3, etc.; R5, R6, R7, R8, R9 = independently H, OH; R10 = H, OPO3H2, OP(O)(OH)R12, OP(O)(OH)OR12; R12 = C1-6 alkyl, Ph, CH2Ph 4-halophenyl, 4-nitrobenzyl, etc.; R11 = A-X-B-Y-C-R13; A, B, C = independently Ph, furanyl, thiophenyl, 6 membered N-contg.-heterocyclyl; X, Y = independently bond, C.tplbond.C; R13 = C1-12 alkyl, C1-12 alkoxy, O-(CH2)m-[O-(CH2)n]p-O-(C1-12 alkyl); m, n = 2-4; p = 0, 1] or a pharmaceutically acceptable salt thereof, were prepd. as antifungal and antiparasitic agents. In particular, echinocandin cyclic deriv. compds. and pharmaceutical compns. thereof, are disclosed. For example, acylation of antibiotic A-30912A nucleus (II, R14 = H) with the N1-hydroxybenzotriazole ester of HO-Q1 (prepn. given) in DMF gave II (R14 = Q1). Prepd. agents I inhibited C albicans in vitro in mice with MIC values of 0.78 to .002 .mu.g/mL and in vivo in mice with ED50 values of >2.5 to 0.31 mg/kg.

IC ICM A61K038-12
ICS C07K005-00

CC 34-3 (Amino Acids, Peptides, and Proteins)
Section cross-reference(s): 1, 10

ST cyclic peptide semisynthesis antifungal antiparasitic; antibiotic A30912A analog prepn fungicide; echinocandin analog prepn antifungal antiparasitic

IT Peptides, preparation
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(cyclic; semisynthesis of cyclic peptide antifungal and

antiparasitic agents)
IT Fungicides
Parasiticides
(semisynthesis of cyclic peptide antifungal and antiparasitic agents)
IT Pneumocystis carinii
(semisynthesis of cyclic peptides for treatment of Pneumocystis carinii infections)
IT 194482-18-3P 194482-19-4P 194482-20-7P 194482-21-8P
194482-22-9P 194482-23-0P 194482-24-1P 194482-25-2P
194482-26-3P 194482-27-4P 194482-28-5P 194482-29-6P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(semisynthesis of cyclic peptide antifungal and antiparasitic agents)
IT 585-70-6 619-44-3, Methyl 4-iodobenzoate 624-28-2, 2,5-Dibromopyridine 763-69-9 5326-23-8, 6-Chloronicotinic acid 5419-55-6, Triisopropyl borate 5751-82-6 19812-93-2 38353-06-9 71849-58-6, Hydroxybenzotriazole 79411-15-7, Antibiotic A-30912A nucleus
RL: RCT (Reactant); RACT (Reactant or reagent)
(semisynthesis of cyclic peptide antifungal and antiparasitic agents)
IT 2527-99-3P 25307-87-3P 30752-18-2P 32779-36-5P 33458-27-4P
40501-41-5P 54769-22-1P 63619-51-2P 65488-27-9P 73781-91-6P
89793-12-4P 91978-81-3P 123732-04-7P 136370-19-9P
146449-90-3P 158937-25-8P 185317-24-2P 194481-40-8P
194481-41-9P 194481-43-1P 194481-45-3P 194481-47-5P
194481-49-7P 194481-53-3P 194481-55-5P 194481-59-9P
194481-61-3P 194481-68-0P 194481-74-8P 194481-76-0P
194481-78-2P 194481-80-6P 194481-82-8P 194481-84-0P
194481-86-2P 194481-88-4P 194481-90-8P 194481-91-9P
194481-92-0P 194481-93-1P 194481-94-2P 194481-95-3P
194481-96-4P 194481-97-5P 194481-98-6P 194481-99-7P
194482-00-3P 194482-01-4P 194482-02-5P 194482-03-6P
194482-04-7P 194482-05-8P 194482-06-9P 194482-07-0P
194482-08-1P 194482-09-2P 194482-10-5P 194482-11-6P
194482-12-7P 194482-13-8P 194482-14-9P 194482-15-0P
194482-16-1P 194482-17-2P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(semisynthesis of cyclic peptide antifungal and antiparasitic agents)

L36 ANSWER 12 OF 17 MARPAT COPYRIGHT 2003 ACS
ACCESSION NUMBER: 126:212437 MARPAT
TITLE: Preparation of cyclic peptide antifungal agents
INVENTOR(S): Rodriguez, Michael John
PATENT ASSIGNEE(S): Lilly, Eli, and Co., USA
SOURCE: Eur. Pat. Appl., 22 pp.
CODEN: EPXXDW
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 757058	A1	19970205	EP 1996-305345	19960722
EP 757058	B1	20001108		
R: AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LI, LU, NL, PT, SE				
US 5629289	A	19970513	US 1995-506790	19950725
AT 197460	E	20001111	AT 1996-305345	19960722
ES 2151638	T3	20010101	ES 1996-305345	19960722
WO 9705163	A1	19970213	WO 1996-US12111	19960723
W: AL, AM, AU, AZ, BB, BG, BR, BY, CA, CN, CZ, EE, GE, HU, IL, IS, JP, KE, KG, KP, KR, KZ, LK, LR, LS, LT, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, RO, RU, SD, SG, SI, SK, TJ, TM, TR, TT, UA, UG, US, UZ				
RW: KE, LS, MW, SD, SZ, UG, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
AU 9665938	A1	19970226	AU 1996-65938	19960723
JP 11510165	T2	19990907	JP 1996-507687	19960723
PRIORITY APPLN. INFO.:			US 1995-506790	19950725
			WO 1996-US12111	19960723

OTHER SOURCE(S): CASREACT 126:212437
GI

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

AB Provided are pharmaceutical formulations, and methods of inhibiting fungal and parasitic activity using cyclopeptides I [R11 = H, CH2OH, CHMeOH, CH(OH)CH2CONH2; R12 = H, CH2OH, CHMeOH; R13 = H, Me; R31 = H, OH, OR30; R30 = C1-6 alkyl, PhCH2, (CH2)2SiMe3, CH2CH:CH2, CH2CH(OH)CH2OH, (CH2)aCO2H, (CH2)bNR41R42, (CH2)cPOR43R44, (CH2CH2O)d(C1-6)alkyl; a, b, c = 1-6; R41, R42 = H, C1-6 alkyl; R41R42 = (CH2)e; R43, R44 = OH, C1-6 alkoxy; d = 1, 2; e = 3-5; R32, R21, R22, R23, R24 = OH, H; R0 = OH, OPO3H2, OP(O)(OH)R1, OP(O)(OH)OR1, R1 = C1-6 alkyl, Ph, p-halophenyl, p-nitrophenyl, PhCH2, p-halobenzyl, p-nitrobenzyl; R2 = COC6H4R3; R3 = C6H4R5-4, C.tplbond.CC6H4R6-4, p-C6H4C.tplbond.CC6H4R7-4, p-C6H4C6H4R8-4; R5, R6, R7, R8 = H, C1-12 alkyl, C2-12 alkynyl, C1-12 alkoxy, C1-12 alkylthio, halo, O(CH2)m[O(CH2)n]pO(C1-12 alkyl), O(CH2)qXR4; m = 2-4; n = 2-4; p = 0, 1; q = 2-4; X = pyrrolidino, piperidino, piperazino; R4 = H, C1-12 alkyl, C3-12 cycloalkyl, benzyl, C3-12 cycloalkylmethyl; with the proviso that at least 1 of R11 and R12 must be H] or pharmaceutically acceptable salt thereof. Thus, acylation of 348.1 g (60.2 mmol) antibiotic A 30912A nucleus with 26.0 g (48.2 mmol) terphenyl active ester Me(CH2)4O-p-C6H4-p-C6H4-p-C6H4CO2C6H2Cl3-2,4,5 in 8.5 L of DMF gave 18 g acylated deriv. II (R11 = R12 = CHMeOH, R31 = R32 = OH) (III). Treatment of 5 g III with 17 mL CF3CO2H and 35 mL Et3SiH in 250 mL CH2Cl2 gave 3.872 g (79%) reduced deriv. II (R11 = R12 = CHMeOH, R31 = R32 = H), which underwent retro-aldol condensation by treatment with 2.51 g (22.6 mmol) Me3N+O- in 20 mL of a 1:1 mixt. of MeCN and DMF at 100.degree. for 24 h to give 72% II (R11 = R12 = R31 = R32 = H). Pharmaceutical formulations contg. II (R11 = R12 = R31 = R32 = H) arte given.

IC ICM C07K007-56
ICS A61K038-12

CC 34-3 (Amino Acids, Peptides, and Proteins)

Section cross-reference(s): 1, 10, 63

ST echinocandin B analog prepn antifungal agent; retro aldol echinocandin deriv trimethylamine oxide; amine oxide retro aldol echinocandin deriv

IT Fungicides
(prepn. of echinocandin derivs. as antifungal agents)

IT Aldol condensation
(retro; prepn. of echinocandin derivs. as antifungal agents)

IT 54651-05-7DP, Echinocandin B, derivs. 179118-66-2P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of echinocandin derivs. as antifungal agents)

IT 1184-78-7, Trimethylamine oxide 2687-45-8, Triethylamine oxide 79411-15-7, Antibiotic A 30912A nucleus 136449-78-0 136449-79-1, Ethanamine, N,N-diethyl-, N-oxide, monohydrate 158937-65-6
RL: RCT (Reactant); RACT (Reactant or reagent)
(prepn. of echinocandin derivs. as antifungal agents)

IT 166663-25-8P 179118-65-1P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(prepn. of echinocandin derivs. as antifungal agents)

L36 ANSWER 13 OF 17 MARPAT COPYRIGHT 2003 ACS

ACCESSION NUMBER: 126:75252 MARPAT

TITLE: Semisynthesis of cyclic peptide antifungal agents

INVENTOR(S): Jamison, James Andrew; Rodriguez, Michael John; Lagrandeur, Lisa Marie Hammond; Turner, William Wilson, Jr.; Zweifel, Mark James

PATENT ASSIGNEE(S): Lilly, Eli, and Co., USA

SOURCE: Eur. Pat. Appl., 55 pp.
CODEN: EPXXDW

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 744405	A2	19961127	EP 1996-303602	19960521
EP 744405	A3	19980527		
R: AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LI, LU, NL, PT, SE				
US 5652213	A	19970729	US 1996-613949	19960311
CA 2220728	AA	19961128	CA 1996-2220728	19960520
WO 9637510	A1	19961128	WO 1996-US7244	19960520
W: AL, AM, AU, AZ, BB, BG, BR, BY, CA, CN, CZ, EE, GE, HU, IS, JP, KE, KG, KP, KR, KZ, LK, LR, LS, LT, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, RO, RU, SD, SG, SI, SK, TJ, TM, TR, TT, UA, UG, US, UZ, VN				
RW: KE, LS, MW, SD, SZ, UG, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
AU 9657991	A1	19961211	AU 1996-57991	19960520
ZA 9604014	A	19971120	ZA 1996-4014	19960520
JP 11505845	T2	19990525	JP 1996-535782	19960520
PRIORITY APPLN. INFO.:			US 1995-453052	19950526

WO 1996-US7244 19960520

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* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

AB Provided are pharmaceutical formulations, and methods of inhibiting fungal and parasitic activity using compds. I [R1 = H, Me, CH2CONH2; R2, R3 = independently H, Me; R4 = H, OH, OR; R = C1-6 alkyl, CH2Ph, (CH2)2SiMe3, CH2CH(OH)CH2OH, CH2CH:CH2, (CH2)aCO2H, (CH2)bNR12R13, (CH2)cPOR14R15, (CH2CH2O)d(C1-6 alkyl); a, b, c = independently 1-6; R12, R13 = independently H, C1-6 alkyl; R12R13 = (CH2)e; R14, R15 = independently OH, C1-6 alkoxy; d = 1, 2; e = 3-5; R5, R6, R7, R8, R9 = independently H, OH; R10 = OH, OPO3H2, OP(O)(OH)R1, OP(O)(OH)OR16; R16 = C1-6 alkyl, Ph, 4-halophenyl, 4-O2NC6H4, PhCH2, 4-halobenzyl, 4-O2NC6H4CH2; R11 = substituted Ph, naphthyl, Q, (un)substituted benzo[c]phenanthrenyl, (C1-12 alkyl)-OC6H4Ph-4; R17 = C1-12 alkoxy, O(CH2)m[O(CH2)n]pO(C1-12 alkyl), m = 2-4; n = 2-4; p = 0, 1], or a pharmaceutically acceptable salt thereof. Thus, acylation of 348.1 g antibiotic A-30912A nucleus (II; R18 = R19 = H) with 26.0 g terphenyl active ester 2,4,5-Cl3C6H2O-Q1 (prepn. given) in 8 L DMF gave 18 g. title compd. II (R18 = Q1, R19 = H) (III). III was converted into O-alkylated derivs. I [R18 = Q1, R19 = CH2CH:CH2, CH2CH(OH)CH2OH, CH2CO2H, (CH2)4NH2, (CH2)6NH2, CH2CH2NH2, etc.]. Selected compds. II inhibited C. albicans in vitro with MIC values of 0.625 to 0.0098 .mu.g/mL, and in vivo in mice with ED50 values of >2.5 to 0.312 mg/kg.

IC ICM C07K007-56
ICS A61K038-12

CC 34-3 (Amino Acids, Peptides, and Proteins)
Section cross-reference(s): 1, 10, 63

ST cyclic peptide semisynthesis antifungal agent; acylation alkylation antibiotic A30912A nucleus; echinocandin alkylated acylated analog prepn fungicide

IT Fungicides
(semisynthesis of cyclic peptide antifungal agents)

IT 158936-15-3P 166663-25-8P 185425-41-6P 185425-42-7P
185425-43-8P 185425-44-9P 185425-45-0P 185425-49-4P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
(semisynthesis of cyclic peptide antifungal agents)

IT 158935-96-7P 158935-97-8P 158935-98-9P 158936-00-6P
158936-01-7P 158936-02-8P 158936-03-9P 158936-04-0P
158936-05-1P 158936-06-2P 158936-07-3P 158936-08-4P
158936-09-5P 158936-10-8P 158936-11-9P 158936-12-0P
158936-13-1P 158936-14-2P 158936-16-4P 158936-19-7P
158936-20-0P 158936-21-1P 158936-67-5P 158936-68-6P
158936-69-7P 158936-70-0P 158936-71-1P 158936-72-2P
166663-26-9P 166663-28-1P 166663-53-2P 166663-55-4P
166663-56-5P 183211-55-4P 183211-56-5P 183211-57-6P
183211-58-7P 183211-59-8P 183211-60-1P 183211-61-2P
185425-40-5P 185425-46-1P 185425-47-2P 185425-48-3P
185425-50-7P 185425-51-8P 185425-52-9P 185425-53-0P
185425-54-1P 185425-55-2P 185425-56-3P 185425-57-4P

185425-58-5P 185425-59-6P 185425-60-9P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(semisynthesis of cyclic peptide antifungal agents)

IT 79-14-1, reactions 95-95-4, 2,4,5-Trichlorophenol 100-51-6, Benzyl alcohol, reactions 106-94-5, 1-Bromopropane 107-18-6, 3-Hydroxypropene, reactions 107-82-4, Isoamyl bromide 108-01-0 110-53-2, 1-Bromopentane 111-25-1, 1-Bromohexane 111-66-0, 1-Octene 111-90-0, 2-(2-Ethoxyethoxy)ethanol 120-47-8, Ethyl 4-hydroxybenzoate 536-74-3, Phenylacetylene 540-38-5, 4-Iodophenol 542-69-8, 1-Iodobutane 619-44-3, Methyl 4-iodobenzoate 629-05-0, 1-Octyne 693-02-7, 1-Hexyne 764-93-2, 1-Decyne 1066-54-2, (Trimethylsilyl)acetylene 1647-26-3, 2-Bromoethylcyclohexane 2002-24-6, Ethanolamine hydrochloride 2038-91-7, 3-Bromofluorene 2527-99-3, Methyl 5-bromo-2-furancarboxylate 2893-43-8 2893-48-3 2916-68-9, 2-(Trimethylsilyl)ethanol 2955-88-6, 1-(2-Hydroxyethyl)pyrrolidine 3034-86-4, Methyl 4-ethynylbenzoate 3814-34-4, 3-(Bromomethyl)pentane 6661-54-7 13295-53-9, Cyclobutylmethyl tosylate 17996-12-2, 6-(Benzyloxycarbonylamino)-1-hexanol 17996-13-3, 4-(Benzyloxycarbonylamino)-1-butanol 19812-93-2, 4-Cyano-4'-hydroxybiphenyl 21856-53-1, Cyclopentylmethyl tosylate 29558-77-8, 4-Bromo-4'-hydroxybiphenyl 40501-41-5, Methyl 4'-hydroxybiphenyl-4-carboxylate 54731-72-5, Dimethyl 2-hydroxyethylphosphonate 60834-63-1 62124-28-1 63619-51-2 63619-63-6 63619-64-7 68880-56-8 79411-15-7, Antibiotic A-30912A nucleus 108366-80-9 131802-89-6 141430-54-8 158407-15-9 158937-22-5 158937-74-7 158937-76-9 158937-77-0 158937-78-1 158937-79-2 158937-80-5 158937-81-6 158937-82-7 158937-83-8 158937-84-9 158937-85-0
RL: RCT (Reactant); RACT (Reactant or reagent)
(semisynthesis of cyclic peptide antifungal agents)

IT 5731-15-7P 25739-23-5P 41424-11-7P 42497-80-3P 52364-71-3P 52709-87-2P 59748-14-0P 59748-15-1P 59748-16-2P 75867-41-3P 82175-72-2P 89752-76-1P 117802-43-4P 117802-44-5P 118788-02-6P 140714-91-6P 144493-15-2P 158936-92-6P 158936-93-7P 158936-95-9P 158936-96-0P 158936-97-1P 158936-98-2P 158936-99-3P 158937-00-9P 158937-01-0P 158937-02-1P 158937-03-2P 158937-04-3P 158937-05-4P 158937-06-5P 158937-07-6P 158937-08-7P 158937-09-8P 158937-10-1P 158937-11-2P 158937-15-6P 158937-16-7P 158937-17-8P 158937-18-9P 158937-19-0P 158937-20-3P 158937-21-4P 158937-23-6P 158937-24-7P 158937-25-8P 158937-26-9P 158937-27-0P 158937-28-1P 158937-29-2P 158937-30-5P 158937-31-6P 158937-32-7P 158937-33-8P 158937-34-9P 158937-35-0P 158937-36-1P 158937-37-2P 158937-38-3P 158937-39-4P 158937-40-7P 158937-41-8P 158937-42-9P 158937-43-0P 158937-44-1P 158937-45-2P 158937-46-3P 158937-47-4P 158937-48-5P 158937-49-6P 158937-50-9P 158937-51-0P 158937-52-1P 158937-53-2P 158937-54-3P 158937-55-4P 158937-56-5P 158937-57-6P 158937-58-7P 158937-59-8P 158937-60-1P 158937-61-2P 158937-62-3P 158937-63-4P 158937-64-5P 158937-65-6P 158937-66-7P 158937-67-8P 158937-68-9P 158937-69-0P 158937-70-3P 158937-71-4P 158937-72-5P 158937-73-6P 158937-86-1P 158937-87-2P 158937-88-3P 158937-89-4P

158937-90-7P 158937-91-8P 158937-92-9P 158937-93-0P
158937-94-1P 158937-95-2P 158937-96-3P 158937-97-4P
158937-98-5P 158937-99-6P 158938-00-2P 158938-01-3P
158938-02-4P 158938-03-5P 158938-04-6P 158938-05-7P
158938-06-8P 158938-07-9P 158938-08-0P 158938-09-1P
158938-10-4P 158938-11-5P 158938-12-6P 158938-13-7P
158938-14-8P 158938-15-9P 158938-16-0P 158938-17-1P
160442-19-3P 183211-53-2P 185425-66-5P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(semisynthesis of cyclic peptide antifungal agents)

L36 ANSWER 14 OF 17 MARPAT COPYRIGHT 2003 ACS
ACCESSION NUMBER: 126:75250 MARPAT
TITLE: Semisynthesis of cyclic peptide antifungal agents
INVENTOR(S): Borromeo, Peter Stanley; Turner, William Wilson
PATENT ASSIGNEE(S): Eli Lilly and Co., USA
SOURCE: Eur. Pat. Appl., 29 pp.
CODEN: EPXXDW
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 744407	A2	19961127	EP 1996-303625	19960521
EP 744407	A3	19980520		
EP 744407	B1	20021009		
R: AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LI, LU, NL, PT, SE				
US 5786325	A	19980728	US 1996-614949	19960311
AU 9657990	A1	19961211	AU 1996-57990	19960320
WO 9637509	A1	19961128	WO 1996-US7243	19960520
W: AL, AM, AU, AZ, BB, BG, BR, BY, CA, CN, CZ, EE, GE, HU, IS, JP, KE, KG, KP, KR, KZ, LK, LR, LS, LT, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, RO, RU, SD, SG, SI, SK, TJ, TM, TR, TT, UA, UG, US, UZ, VN				
RW: KE, LS, MW, SD, SZ, UG, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
ZA 9604011	A	19971120	ZA 1996-4011	19960520
AT 225804	E	20021015	AT 1996-303625	19960521
ES 2180699	T3	20030216	ES 1996-303625	19960521
PRIORITY APPLN. INFO.:			US 1995-451337	19950526
			WO 1996-US7243	19960520

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* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

AB Provided are pharmaceutical formulations, and methods of inhibiting fungal and parasitic activity using compds. I [R1 = H, Me, CH2CONH2; R2, R3 = independently H, Me; R4 = H, OH, OR; R = C1-6 alkyl, CH2Ph, (CH2)2SiMe3, CH2CH(OH)CH2OH, CH2CH:CH2, (CH2)aCO2H, (CH2)bNR12R13, (CH2)cPOR14R15, (CH2CH2O)d(C1-6 alkyl); a, b, c = independently 1-6;

R12, R13 = independently H, C1-6 alkyl; R12R13 = (CH2)e; R14, R15 = independently OH, C1-6 alkoxy; d = 1, 2; e = 3-5; R5, R6, R7, R8, R9 = independently H, OH; R10 = OH, OPO3H2, OP(O)(OH)R1, OP(O)(OH)OR16; R16 = C1-6 alkyl, Ph, 4-halophenyl, 4-O2NC6H4, PhCH2, 4-halobenzyl, 4-O2NC6H4CH2; R11 = C1-12 alkyl, C1-12 alkoxy O(CH2)m[O(CH2)n]pO(C1-12 alkyl); R17 = OH, halo, NO2, NH2, CF3, C1-6 alkyl, C1-6 alkoxy, C1-6 alkylthio; m = 2-4; n = 2-4; p = 0, 1; q = 1-4], or a pharmaceutically acceptable salt thereof. Thus, acylation of antibiotic A-30912A nucleus (II; R18 = H) with substituted triphenylenecarboxylic acid active esters gave title compds. II (R18 = Q; R19 = 2-Cl, 2-Me, 3-Me, 3-MeO, 3-Cl-5-MeO, 3-Cl, 3,5-Me2, 3,5-Cl2, 2,3,5,6-F4, 2-EtO, 2-F). Prepd. fungicides II inhibited C. albicans in vitro with MIC values of 0.039-0.005 .mu.g/mL, and in vivo in mice with ED50 values of >2.5 to 0.39 mg/kg.

IC ICM C07K007-56
ICS A61K038-12

CC 34-3 (Amino Acids, Peptides, and Proteins)
Section cross-reference(s): 1, 10, 63

ST cyclic peptide semisynthesis antifungal agent; echinocandin B analog prepn fungicide; antibiotic A30912A analog prepn fungicide

IT Fungicides
(semisynthesis of cyclic peptide antifungal agents)

IT 185312-61-2P 185312-63-4P 185312-65-6P 185312-67-8P
185312-69-0P 185312-71-4P 185312-73-6P 185312-75-8P
185312-77-0P 185312-79-2P 185312-81-6P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(semisynthesis of cyclic peptide antifungal agents)

IT 106-41-2, 4-Bromophenol 124-63-0, Methanesulfonyl chloride
628-17-1, 1-Iodopentane 2592-95-2, 1-Hydroxybenzotriazole
59748-90-2, 4-Bromo-2-chlorobenzoic acid 79411-15-7, Antibiotic A-30912A nucleus
RL: RCT (Reactant); RACT (Reactant or reagent)
(semisynthesis of cyclic peptide antifungal agents)

IT 54769-22-1P 63619-51-2P 158937-25-8P 185312-82-7P
185312-83-8P 185312-84-9P 185312-85-0P 185312-86-1P
185312-87-2P 185312-88-3P 185312-89-4P 185312-90-7P
185312-91-8P 185312-92-9P 185312-93-0P 185312-94-1P
185312-95-2P 185312-96-3P 185312-97-4P 185312-98-5P
185312-99-6P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(semisynthesis of cyclic peptide antifungal agents)

L36 ANSWER 15 OF 17 MARPAT COPYRIGHT 2003 ACS

ACCESSION NUMBER: 125:329474 MARPAT
TITLE: Preparation of cyclic hexapeptide antifungal agents.
INVENTOR(S): Borromeo, Peter Stanley; Jamison, James Andrew; Rodriguez, Michael John; Turner, William Wilson, Jr.; Vasudevan, Venkatraghavan
PATENT ASSIGNEE(S): Lilly, Eli, and Co., USA
SOURCE: Eur. Pat. Appl., 57 pp.
CODEN: EPXXDW
DOCUMENT TYPE: Patent
LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 736541	A1	19961009	EP 1996-302362	19960403
EP 736541	B1	20021127		
R: AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LI, LU, NL, PT, SE				
US 5646111	A	19970708	US 1996-612208	19960307
ZA 9602598	A	19971001	ZA 1996-2598	19960401
IL 117749	A1	20000601	IL 1996-117749	19960401
CA 2217048	AA	19961010	CA 1996-2217048	19960403
WO 9631228	A1	19961010	WO 1996-US4543	19960403
W: AL, AM, AU, AZ, BB, BG, BR, BY, CA, CN, CZ, EE, GE, HU, IS, JP, KE, KG, KP, KR, KZ, LK, LR, LS, LT, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, RO, RU, SD, SG, SI, SK, TJ, TM, TR, TT, UA, UG, US, UZ, VN				
RW: KE, LS, MW, SD, SZ, UG, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
AU 9653834	A1	19961023	AU 1996-53834	19960403
AU 702841	B2	19990304		
CN 1185739	A	19980624	CN 1996-194199	19960403
BR 9604906	A	19980721	BR 1996-4906	19960403
JP 11504005	T2	19990406	JP 1996-530439	19960403
AT 228535	E	20021215	AT 1996-302362	19960403
NO 9704562	A	19971128	NO 1997-4562	19971002
PRIORITY APPLN. INFO.:			US 1995-418341	19950407
			WO 1996-US4543	19960403

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* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

AB Title compds. [I; R = OP(:O)(OH)R1; R1 = alkyl, alkoxy, Ph, p-halophenyl, p-nitrophenyl, PhO, PhCO, p-halobenzyl, p-nitrobenzyl; R2 = R3C6H4CO R4C6H4ZC6H4CO, etc.; R3 = alkyl, alkoxy, quinolinyl, etc.; Z = O, C.tplbond.C, CH:CH, CH2CH2, CH2, bond; R4 = H, (substituted) alkyl, alkenyl, alkynyl, alkoxy, cycloalkyl, bicycloalkyl, cycloalkoxy, naphthyl, etc.], were prepd. Thus, [I; R = OP(:O)(OH)Bu; R2 = Q1] (prepn. given) showed ED50 = 0.39 mg/kg against Candida albicans in mice.

IC ICM C07K007-56
ICS A61K038-12

CC 34-3 (Amino Acids, Peptides, and Proteins)
Section cross-reference(s): 1

ST cyclopeptide antifungal prepn

IT Fungicides and Fungistats
(prepn. of cyclic hexapeptide antifungal agents)

IT Peptides, preparation
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(cyclo-, prepn. of cyclic hexapeptide antifungal agents)

IT 183211-70-3P 183211-71-4P 183211-72-5P 183211-73-6P

183211-74-7P 183211-75-8P 183211-76-9P 183211-77-0P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of cyclic hexapeptide antifungal agents)

IT 67-63-0, 2-Propanol, reactions 71-36-3, 1-Butanol, reactions 107-08-4, 1-Iodopropane 107-82-4, 1-Bromo-3-Methylbutane 110-53-2, 1-Bromopentane 111-66-0, 1-Octene 536-74-3, Phenylacetylene 542-69-8, n-Butyl iodide 619-44-3, Methyl 4-iodobenzoate 629-05-0, 1-Octyne 638-45-9, 1-Iodohexane 676-97-1, Methylphosphonic dichloride 693-02-7, 1-Hexyne 764-93-2, 1-Decyne 824-72-6, Phenylphosphonic dichloride 1066-50-8, Ethylphosphonic dichloride 1066-54-2, Trimethylsilylacetylene 1647-26-3, 2-Bromoethylcyclohexane 3034-86-4, Methyl 4-ethynylbenzoate 3814-34-4, 1-Bromo-2-ethylbutane 5731-15-7 6661-54-7 13295-53-9, Cyclobutylmethyl tosylate 21856-53-1, Cyclopentylmethyl tosylate 25739-23-5 59748-14-0 59748-15-1 59748-16-2 60834-63-1 62124-28-1 63619-51-2 63619-63-6 63619-64-7 68880-56-8, 3,3-Dimethylbutyl tosylate 79404-91-4, Cilofungin 108366-80-9 117802-43-4 117802-44-5 118788-02-6 140714-91-6 141430-54-8 158937-74-7 158937-76-9 158937-77-0 158937-78-1 158937-79-2 158937-80-5 158937-81-6 158937-82-7 158937-83-8 158937-84-9 158937-85-0 158937-86-1 158937-87-2 158937-88-3 158937-89-4 158937-90-7 158937-91-8 158937-92-9 158937-93-0 158937-94-1 158937-95-2 158937-96-3 158937-97-4 158937-98-5 158937-99-6 158938-00-2 158938-02-4 158938-03-5 158938-04-6 158938-05-7 158938-06-8 158938-07-9 158938-08-0 158938-09-1 158938-10-4 158938-11-5 158938-12-6 158938-13-7 158938-14-8 158938-15-9 158938-16-0 158938-17-1 183211-78-1
RL: RCT (Reactant); RACT (Reactant or reagent)
(prepn. of cyclic hexapeptide antifungal agents)

IT 1498-52-8P, Butyldichlorophosphate 41424-11-7P 42497-80-3P 52364-71-3P 52709-87-2P 56376-11-5P, Isopropyldichlorophosphate 75867-41-3P 82175-72-2P 89752-76-1P 144493-15-2P 144540-63-6P 158935-96-7P 158935-97-8P 158935-98-9P 158936-00-6P 158936-01-7P 158936-02-8P 158936-03-9P 158936-04-0P 158936-05-1P 158936-06-2P 158936-07-3P 158936-08-4P 158936-09-5P 158936-10-8P 158936-11-9P 158936-12-0P 158936-13-1P 158936-14-2P 158936-15-3P 158936-16-4P 158936-19-7P 158936-20-0P 158936-21-1P 158936-46-0P 158936-50-6P 158936-54-0P 158936-62-0P 158936-63-1P 158936-67-5P 158936-68-6P 158936-69-7P 158936-70-0P 158936-71-1P 158936-72-2P 158936-92-6P 158936-93-7P 158936-95-9P 158936-96-0P 158936-97-1P 158936-98-2P 158936-99-3P 158937-00-9P 158937-01-0P 158937-02-1P 158937-03-2P 158937-04-3P 158937-05-4P 158937-06-5P 158937-07-6P 158937-08-7P 158937-09-8P 158937-10-1P 158937-11-2P 158937-14-5P 158937-15-6P 158937-16-7P 158937-17-8P 158937-18-9P 158937-19-0P 158937-20-3P 158937-21-4P 158937-22-5P 158937-23-6P 158937-24-7P 158937-25-8P 158937-26-9P 158937-27-0P 158937-28-1P 158937-29-2P 158937-30-5P 158937-31-6P 158937-32-7P 158937-33-8P 158937-34-9P 158937-35-0P 158937-36-1P 158937-37-2P 158937-38-3P 158937-39-4P 158937-40-7P 158937-41-8P 158937-42-9P 158937-43-0P 158937-44-1P 158937-45-2P 158937-46-3P 158937-47-4P

158937-48-5P 158937-49-6P 158937-50-9P 158937-51-0P
158937-53-2P 158937-54-3P 158937-55-4P 158937-56-5P
158937-57-6P 158937-58-7P 158937-59-8P 158937-60-1P
158937-61-2P 158937-62-3P 158937-63-4P 158937-64-5P
158937-65-6P 158937-66-7P 158937-67-8P 158937-68-9P
158937-69-0P 158937-70-3P 158937-71-4P 158937-72-5P
158937-73-6P 160442-19-3P 166663-25-8P 166663-26-9P
166663-28-1P 166663-53-2P 166663-55-4P 166663-56-5P
179118-65-1P 183211-53-2P 183211-54-3P 183211-55-4P
183211-56-5P 183211-57-6P 183211-58-7P 183211-59-8P
183211-60-1P 183211-61-2P 183211-62-3P 183211-63-4P
183211-64-5P 183211-65-6P 183211-66-7P 183211-67-8P
183211-68-9P 183211-69-0P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(prepn. of cyclic hexapeptide antifungal agents)

L36 ANSWER 16 OF 17 MARPAT COPYRIGHT 2003 ACS
ACCESSION NUMBER: 124:146869 MARPAT
TITLE: Preparation of cyclopeptide antifungal and anti-pneumocystis compounds.
INVENTOR(S): Balkovec, James M.; Bouffard, Frances Aileen; Black, Regina M.
PATENT ASSIGNEE(S): Merck and Co., Inc., USA
SOURCE: PCT Int. Appl., 81 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9527074	A1	19951012	WO 1995-US3948	19950331
W: AM, AU, BB, BG, BR, BY, CA, CN, CZ, EE, FI, GE, HU, IS, JP, KG, KR, KZ, LK, LR, LT, LV, MD, MG, MN, MX, NO, NZ, PL, RO, RU, SG, SI, SK, TJ, TT, UA, UZ				
RW: KE, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
US 5541160	A	19960730	US 1994-222157	19940404
AU 9521307	A1	19951023	AU 1995-21307	19950331
PRIORITY APPLN. INFO.:			US 1994-222157	19940404
			WO 1995-US3948	19950331

GI

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

AB Title compds. [I; R = alkyl, alkenyl, Ph, biphenyl, naphthyl, terphenyl, alkylamino, dialkylamino, alkoxyaryl; R1, R2, R4 = H, OH; R3 = H, OH, O(CH2)nNRVRVI (RV, RVI, RVII = H, alkyl), O(CH2)nNRVRVIRVII+Y-; n = 2-6; Y = counterion; R5 = H, Me, OH; R6 = H, Me; R7 = H, Me, CH2C(:O)NH2, (CH2)2NRVRVI, (CH2)2NRVRVIRVII+Y-; R8 = Cl, Br, iodo, NO2, N3, (CH2)0-4NH2, (CH2)0-4NHalkyl, (CH2)0-4N(alkyl)2, (CH2)0-3CH(:NOH), NHC(:O)(CH2)1-6NH2,

NHC(:O)(CH2)1-6NHC(:NH)(CH2)0-3H], were prepd. Thus, title compd. (II) (prepd. from pneumocandin B0) showed a min. fungicidal concn. of 0.25 .mu.g/mL against Candida albicans MY1055.

IC ICM C12P021-04

CC 34-3 (Amino Acids, Peptides, and Proteins)
Section cross-reference(s): 1, 10

ST echinocandin analog prepn antifungal; pneumocandin analog prepn antifungal; cyclopeptide prepn antifungal

IT Pneumocystis
(infection treatment; prepn. of cyclopeptide antifungal and anti-pneumocystis compds.)

IT Fungicides and Fungistats
(prepn. of cyclopeptide antifungal and anti-pneumocystis compds.)

IT Peptides, preparation
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(cyclo-, prepn. of cyclopeptide antifungal and anti-pneumocystis compds.)

IT 173305-50-5P 173305-51-6P 173305-52-7P 173305-53-8P
173305-54-9P 173305-55-0P 173305-56-1P 173305-57-2P
173305-59-4P 173305-60-7P 173305-62-9P 173305-64-1P
173305-66-3P 173305-68-5P 173305-70-9P 173305-71-0P
173305-72-1P 173305-73-2P 173305-74-3P 173305-75-4P
173305-76-5P 173305-77-6P 173305-78-7P 173305-79-8P
173305-80-1P 173305-81-2P 173305-82-3P 173305-83-4P
173397-50-7P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of cyclopeptide antifungal and anti-pneumocystis compds.)

IT 110-53-2, n-Pentyl bromide 619-42-1, Methyl 4-bromobenzoate 2208-07-3, Ethyl acetimidate hydrochloride 5470-11-1, Hydroxylamine hydrochloride 16748-79-1, Z-Gly-OPfp 24850-33-7, Allyltributyltin 29558-77-8, 4-(4-Bromophenyl)phenol 71018-21-8 77987-49-6 79411-15-7 135575-42-7, Pneumocandin B0 138516-82-2 150167-56-9
RL: RCT (Reactant); RACT (Reactant or reagent)
(prepn. of cyclopeptide antifungal and anti-pneumocystis compds.)

IT 63619-51-2P 158937-25-8P 158937-30-5P 158938-08-0P
166663-25-8P 173305-84-5P 173305-85-6P 173305-86-7P
173305-87-8P 173305-88-9P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(prepn. of cyclopeptide antifungal and anti-pneumocystis compds.)

L36 ANSWER 17 OF 17 MARPAT COPYRIGHT 2003 ACS
ACCESSION NUMBER: 122:82078 MARPAT
TITLE: Cyclic peptide antifungal agents and process for preparation thereof
INVENTOR(S): Burkhardt, Frederick Joseph; Debono, Manuel; Nissen, Jeffrey Scott; Turner, William Wilson, Jr.
PATENT ASSIGNEE(S): Lilly, Eli, and Co., USA
SOURCE: Eur. Pat. Appl., 56 pp.
CODEN: EPXXDW

DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 561639	A1	19930922	EP 1993-302064	19930318
EP 561639	B1	20020515		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, NL, PT, SE				
CA 2091663	AA	19930920	CA 1993-2091663	19930315
ZA 9301830	A	19940915	ZA 1993-1830	19930315
IL 105048	A1	20010614	IL 1993-105048	19930315
NZ 299314	A	20010928	NZ 1993-299314	19930315
CZ 288974	B6	20011017	CZ 1993-416	19930315
IL 122315	A1	20020310	IL 1993-122315	19930315
NO 9300948	A	19930920	NO 1993-948	19930316
BR 9301232	A	19930921	BR 1993-1232	19930318
HU 63637	A2	19930928	HU 1993-785	19930318
CN 1080926	A	19940119	CN 1993-103587	19930318
CN 1036715	B	19971217		
JP 06056892	A2	19940301	JP 1993-58529	19930318
RU 2129562	C1	19990427	RU 1993-4787	19930318
AT 217635	E	20020615	AT 1993-302064	19930318
JP 2002226500	A2	20020814	JP 2002-3969	19930318
ES 2174843	T3	20021116	ES 1993-302064	19930318
AU 9335341	A1	19930923	AU 1993-35341	19930319
AU 9665529	A1	19961205	AU 1996-65529	19960909
AU 689391	B2	19980326		
PRIORITY APPLN. INFO.:			US 1992-854117	19920319
			US 1992-992390	19921216
			IL 1993-105048	19930315
			JP 1993-58529	19930318

GI

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

AB Title compds. (I; R, R11 = independently H, OH; R1 = H, OH, OSO3H; R2 = substituted PhCO, biphenylyl, naphthoyl, etc.; R7 = R1, phosphonooxy; R8 = H, Me, H2NCOCH2; R9, R10 = Me, H), were prepd. Thus, I (R = R7 = R11 = OH, R1 = H, R2 = Q1, R8 = R9 = R10 = Me), prepd. by enzymic deacylation and then reacylation of echinocandin B, showed ED50 = 0.84 mg/mL for controlling systemic fungal infections in mice. Several I were effective against Pneumocystis carinii in immunosuppressed rats. I in general exhibit oral bioavailability.

IC ICM C07K007-56
ICS A61K037-02

CC 34-3 (Amino Acids, Peptides, and Proteins)
Section cross-reference(s): 1

ST peptide cyclic prepn medical fungicide; echinocandin analog prepn medical fungicide

IT Fungicides and Fungistats
(cyclic peptide derivs)

IT Peptides, preparation
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(cyclo-, prepn. of, as medical fungicides)

IT 79411-15-7
RL: RCT (Reactant); RACT (Reactant or reagent)
(acylation of, in prepn. of medical fungicide)

IT 5731-15-7P 25739-23-5P 41424-11-7P 42497-80-3P 52364-71-3P
52709-87-2P 59748-14-0P 59748-15-1P 59748-16-2P 75867-41-3P
82175-72-2P 89752-76-1P 117802-43-4P 117802-44-5P
118788-02-6P 140714-91-6P 144493-15-2P 144540-61-4P
158936-92-6P 158936-93-7P 158936-94-8P 158936-95-9P
158936-96-0P 158936-97-1P 158936-98-2P 158936-99-3P
158937-00-9P 158937-01-0P 158937-02-1P 158937-03-2P
158937-04-3P 158937-05-4P 158937-06-5P 158937-07-6P
158937-08-7P 158937-09-8P 158937-10-1P 158937-11-2P
158937-12-3P 158937-13-4P 158937-14-5P 158937-15-6P
158937-16-7P 158937-17-8P 158937-18-9P 158937-19-0P
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158937-24-7P 158937-25-8P 158937-26-9P 158937-27-0P
158937-28-1P 158937-29-2P 158937-30-5P 158937-31-6P
158937-32-7P 158937-33-8P 158937-34-9P 158937-35-0P
158937-36-1P 158937-37-2P 158937-38-3P 158937-39-4P
158937-40-7P 158937-41-8P 158937-42-9P 158937-43-0P
158937-44-1P 158937-45-2P 158937-46-3P 158937-47-4P
158937-48-5P 158937-49-6P 158937-50-9P 158937-51-0P
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158937-56-5P 158937-57-6P 158937-58-7P 158937-59-8P
158937-60-1P 158937-61-2P 158937-62-3P 158937-63-4P
158937-64-5P 158937-65-6P 158937-66-7P 158937-67-8P
158937-68-9P 158937-69-0P 158937-70-3P 158937-71-4P
158937-72-5P 158937-73-6P 158937-86-1P 158937-87-2P
158937-88-3P 158937-89-4P 158937-90-7P 158937-91-8P
158937-92-9P 158937-93-0P 158937-94-1P 158937-95-2P
158937-96-3P 158937-97-4P 158937-98-5P 158937-99-6P
158938-00-2P 158938-01-3P 158938-02-4P 158938-03-5P
158938-04-6P 158938-05-7P 158938-06-8P 158938-07-9P
158938-08-0P 158938-09-1P 158938-10-4P 158938-11-5P
158938-12-6P 158938-13-7P 158938-14-8P 158938-15-9P
158938-16-0P 158938-17-1P 160442-19-3P
RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn. of, as intermediate for cyclic peptide deriv medical fungicide)

IT 158935-94-5P 158935-95-6P 158935-96-7P 158935-97-8P
158935-98-9P 158935-99-0P 158936-00-6P 158936-01-7P
158936-02-8P 158936-03-9P 158936-04-0P 158936-05-1P
158936-06-2P 158936-07-3P 158936-08-4P 158936-09-5P
158936-10-8P 158936-11-9P 158936-12-0P 158936-13-1P
158936-14-2P 158936-15-3P 158936-16-4P 158936-17-5P
158936-18-6P 158936-19-7P 158936-20-0P 158936-21-1P
158936-22-2P 158936-23-3P 158936-24-4P 158936-25-5P
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158936-34-6P 158936-35-7P 158936-36-8P 158936-37-9P
158936-38-0P 158936-39-1P 158936-40-4P 158936-41-5P
158936-42-6P 158936-43-7P 158936-44-8P 158936-45-9P